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OF
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THIRD SERIES FOUNDED BY EDWARD JACKSON

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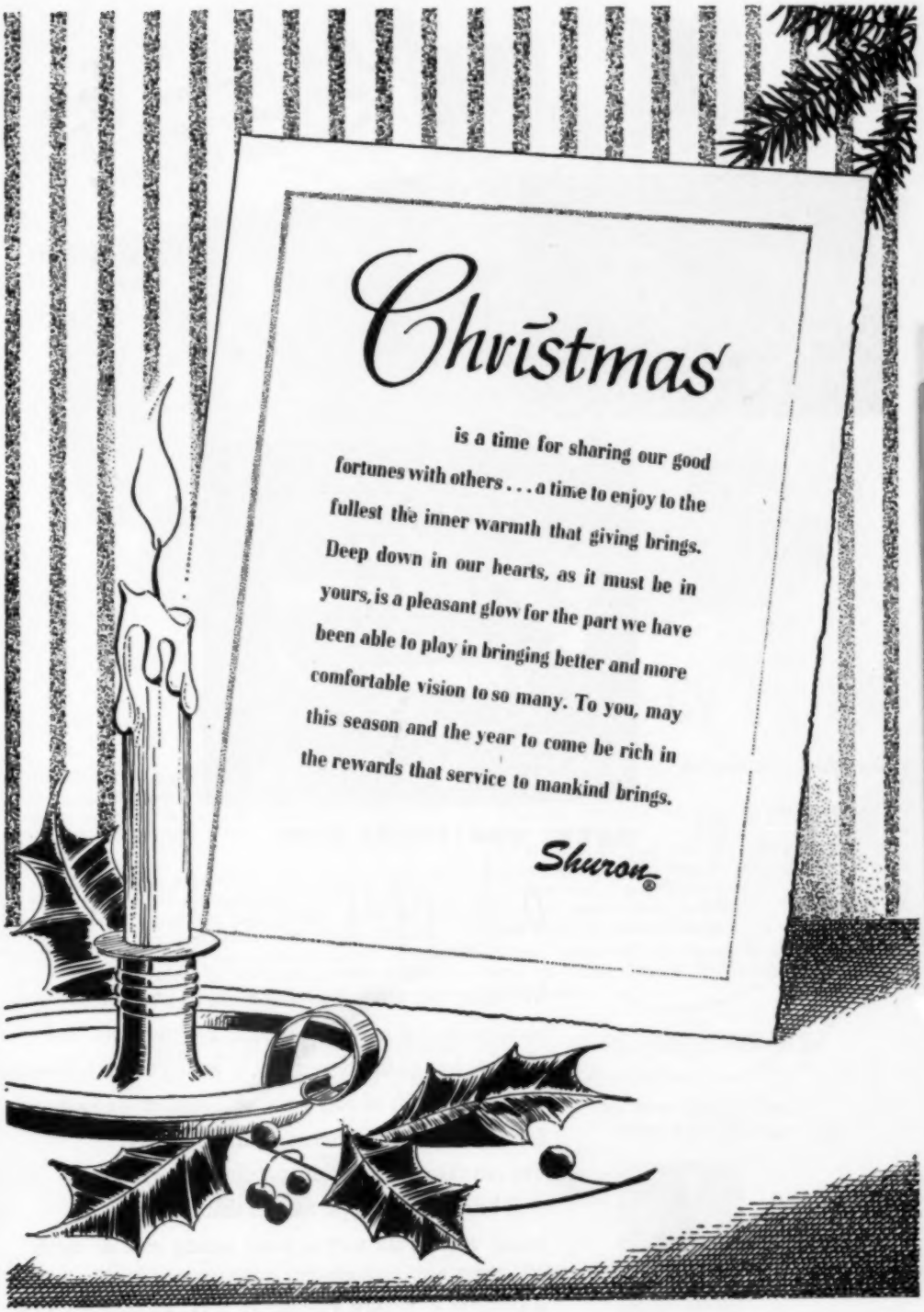
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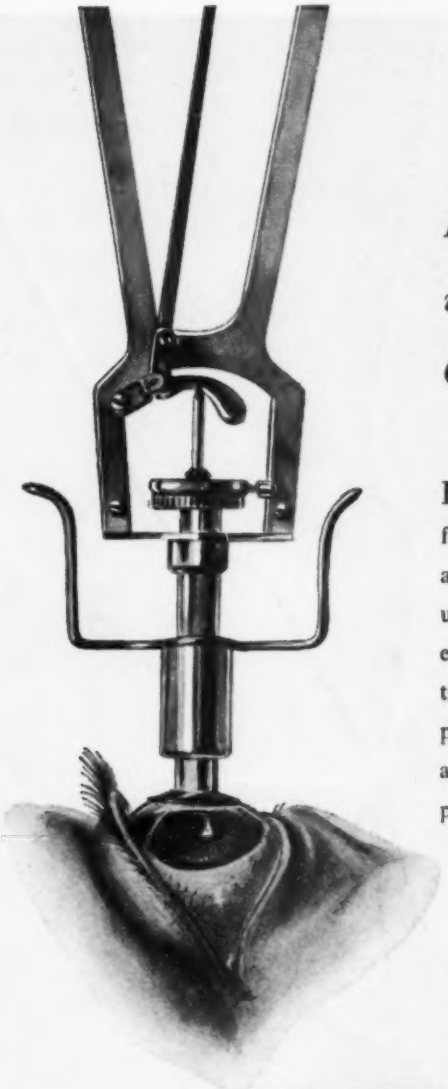

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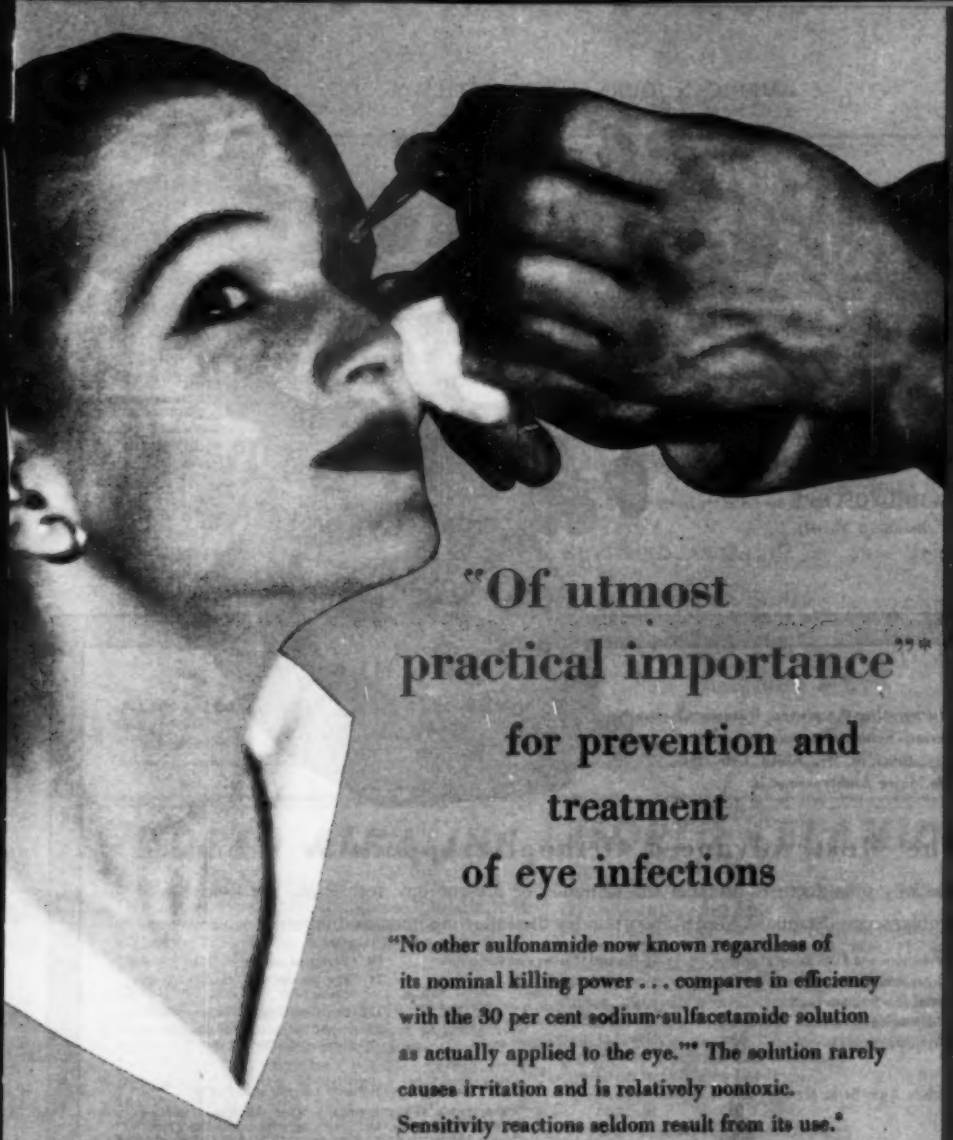

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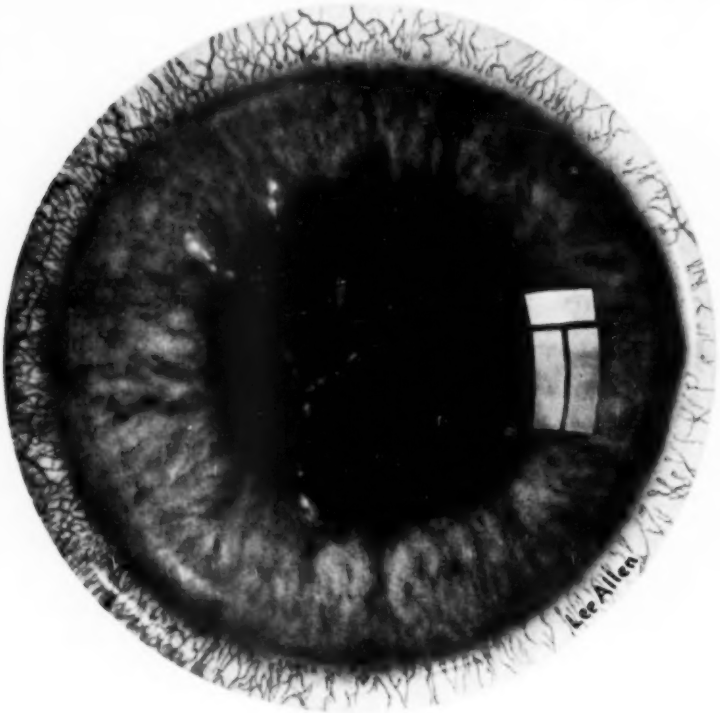

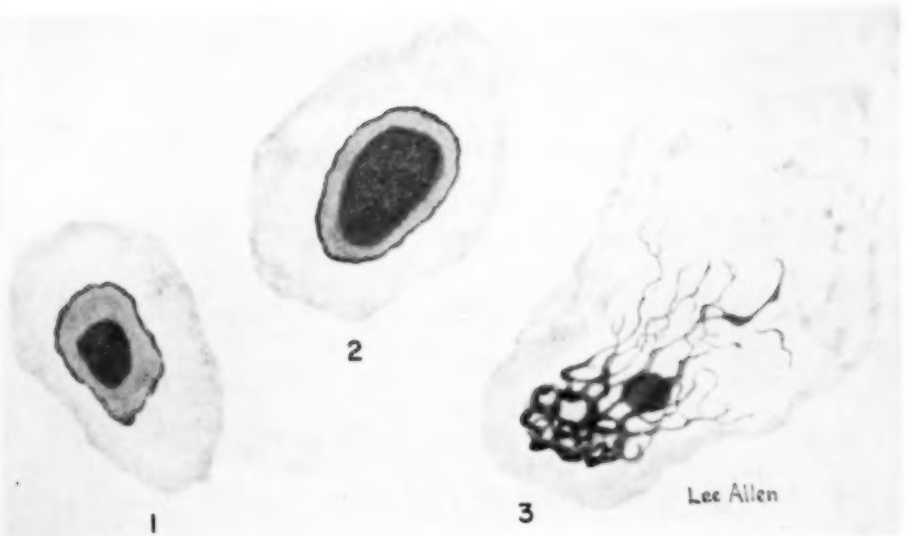

FIGS. 1 AND 2 (BRALEY). (FIG. 1) DENDRITIC ULCER. (FIG. 2) (1 AND 2) INTRANUCLEAR INCLUSION OF HERPES-SIMPLEX VIRUS IN SECTION. HEMATOXYLIN-EOSIN STAIN. (3) INTRANUCLEAR INCLUSION OF HERPES-SIMPLEX VIRUS IN BROKEN EPITHELIAL-CELL NUCLEUS.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 35 DECEMBER, 1952 NUMBER 12

EXPERIMENTAL HERPES SIMPLEX*

THE SANFORD R. GIFFORD LECTURE

ALSON E. BRALEY, M.D.
Iowa City, Iowa

It is an unique honor to deliver the eighth annual Gifford Memorial Lecture. I am sure that Sanford Robinson Gifford, who would have been 60 years old now, might have enjoyed this lecture. His first interest was ophthalmic bacteriology, in which he constantly tried to combine clinical observations with laboratory findings. He was active in laboratory research in an effort to explain clinical disease. I will attempt to present some new concepts regarding clinical and experimental herpes simplex, which may explain some of the strange and sometimes baffling clinical findings.

Herpes is a confusing clinical term from the Greek word "herpein" meaning to creep. Clinically it implies a cluster of small vesicles on the skin or mucous membrane which tend to spread or creep in the epithelium. Vidal,[1] in 1873, was probably the first to show that the herpes-simplex lesions on the lips were infectious. It remained for an ophthalmologist, Grüter,[2] in 1912, to show that the lesions on lips and cornea were similar, and produced identical changes on a rabbit cornea. The intranuclear inclusions were described by Lipschütz,[3] Loewenstein,[4] and Grüter,[5] as well as others between 1912 and 1920, but as late as 1938 Doerr[6] held that herpes simplex was not a virus infection at all, but a queer physiologic response of the cells to fever and other irritation. He considered the disease so strange that it could not be a virus disease.

When Lipschütz[3] described the acidophilic intranuclear inclusion as "alpha bodies," Doerr and others considered them of no importance. It remained for Burnet and Lush,[7] Goodpasture and Teague[8] and many others to show that herpes simplex is a virus disease and could be "brought into line with other infectious virus diseases."[9]

The disease is not easily "brought into line" as you will see. In order briefly to visualize a herpes infection, let us accept a few statements. The first herpes-simplex infection takes place in infancy or childhood as an aphthous stomatitis. The virus then remains in the mouth for life. At the same time a conjunctivitis may also occur, or the conjunctivitis may occur without the stomatitis. Likewise the infection persists for life. Most of the time the infection is entirely latent, but certain stimuli may call the virus into activity and allow it to be reliberated into susceptible tissue.

The results of research by Burnet[9] and his co-workers have shown that individuals susceptible to herpes have circulating serum antibodies to the virus. They have shown that antibody titration can be done on the chorioallantoic membrane of developing hens' eggs.

If one measures the antibodies to most infectious diseases in the serum, one finds in a population a continuous range from no antibody to very high titers. With herpes simplex they reported an "all or nothing" response. Either the antibody titer is very high or there is none.

* From the Department of Ophthalmology, State University of Iowa. Presented before the Chicago Ophthalmological Society, February, 1952

In a study of a worldwide population cross section, certain classes show larger numbers with serum antibodies. Herpes simplex is prevalent in 90 percent of lower classes of people, while in higher classes, such as in university students, only 30 percent to 35 percent will have antibodies.

The adults who are susceptible have repeated attacks, while those who are not almost never develop the infection. Similarly persons who are not susceptible have no serum antibody.

In general herpes simplex is an unimportant disease. However, in the eye it is extremely important and may destroy sight. A number of eyes are lost every day from this infection.

Clinical types of infection

Clinically in the eye I recognize four types of infection:

1. An acute primary herpes-simplex blepharokeratoconjunctivitis.
2. Self-limited, recurrent dendritic ulcers of the cornea without conjunctivitis.
3. A dendritic ulcer of the cornea which progresses to the development of a disciform keratitis and uveitis.
4. A chronic keratitis with some dendritic ulcer character, with active and healed areas, which may be called keratitis metaherpetica.

Acute primary keratoconjunctivitis (herpes simplex)

This infection is characterized by an acute or hyperacute keratoconjunctivitis. It usually begins suddenly with edema of the lids and bulbar conjunctiva. Blisters usually develop on the lid border and the conjunctiva becomes beady with follicles. A preauricular lymph node is present, and there may be many lymph nodes in the anterior cervical chain. There may be an associated rhinitis and stomatitis. The cornea usually shows a distinct dendritic figure, but it is not unusual that the corneal epithelium is entirely denuded. Occasionally multiple dendritic figures are present. The disease runs a course of 14 to 18 days, and heals with slight scarring in the cornea.

This acute disease usually occurs in the teen ages, between the 12th and the 19th years. I have, however, seen it occur in children two years of age, and two cases in women aged 29 and 34.

In older individuals the disease is likely to become a chronic keratitis, while in children and teenagers the disease is self-limited. After the initial acute attack, the disease may pass into one of the other forms of the disease.

The virus may easily be isolated during the acute phase of the disease, as was shown by Maumenee, Hayes, and Hartman.[10] We have isolated the herpes-simplex virus on two occasions, once from a teen-age girl and again from a 29-year-old woman. The viruses were isolated by the tissue-culture technique, which has been described previously.[11]

These patients have no serum antibodies during the acute phase of the disease. Antibodies slowly develop after the disease has run its course or becomes chronic, and at the end of 30 days definite titers can be measured by mouse neutralization tests. It takes about 60 days before the highest titers can be demonstrated.

Recurrent dendritic ulcers of the cornea without conjunctivitis

This disease is the most common form of the infection and has been extensively covered by Gundersen.[12] It develops suddenly, with a slight foreign-body sensation. When the lesion is first seen, the bulbar conjunctival vessels are slightly injected and the cornea shows a narrow linear line composed of whitish nodules in the epithelium. This line forms into the typical branching figure (fig. 1).

Beneath the line of whitish nodules is the gray infiltrate. When the lesion is stained with fluorescein, the fine line in the epithelium takes a brilliant green stain.

I believe that an individual who develops this lesion must have the virus in his conjunctival sac at all times. The virus lies dormant

or latent in the cells, but may be released and produce a typical dendritic ulcer under appropriate conditions. These conditions vary with the individual.

I think that most of these patients have had an acute or subacute conjunctivitis in infancy, either with or without a stomatitis. Recurrent attacks of dendritic keratitis will then occur. These lesions run a course of five to 14 days and heal, leaving a slight scar in Bowman's membrane.

The virus then returns to its latent state in the cells, awaiting the proper stimulus to produce another lesion. The stimuli come from several sources. One source of stimuli is the action of radiant energy on the eye.

The effect of infrared and ultraviolet on the corneal epithelial cells has been described by Duke-Elder.[13] He showed the marked nuclear changes produced in the corneal epithelium.

Since the herpes simplex virus lies dormant in the nucleus of these epithelial cells, it could be released to produce a dendritic ulcer. We are all well acquainted with the severe herpes labialis which develops after a sunburn of the face.

A number of case reports demonstrate that dendritic ulcers form after arc-flash burns of the cornea. Trauma also produces herpes labialis, and since the keratitis is comparable, then trauma to the cornea must play an important role in the development of dendritic ulcer.

One of the most potent stimuli producing herpes corneae is fevers. Malaria frequently produces fever blisters and dendritic ulcers, and all ophthalmologists are familiar with the fever blisters that follow intravenous typhoid injections.

Although fever blisters on the lips are well known following intravenous killed typhoid bacilli, dendritic ulcers are not so prevalent. They do occur, however, and the proportion is about the same as for the general population. A little more than 50 percent of the population develops herpes labialis, while only one in 1,000 develops herpes corneae.

The mechanism of release of the herpes virus from the nucleus to produce its infection is not well understood. You can see in sections of the corneal epithelium the typical eosinophilic intranuclear inclusion bodies are completely surrounded by the dense nuclear membrane (fig. 2—1 and 2). Any substance that will interfere with this nuclear membrane may release the virus. When the virus is released, however, it may be completely neutralized by the fixed tissue antibody. The presence of this fixed tissue antibody (aggressin) has been demonstrated by many authors.*

Although we have not proven the presence of this neutralizing substance in the immune cornea, we are quite sure some substance exists. The balance between this local immune substance and the virus is critical, and the immune substances may be destroyed by some enzyme action.

One of the substances that disturbs the local immunity is cortisone. Cortisone applied to the cornea at the beginning of a dendritic ulcer will spread the lesion to the entire cornea.[14] From my experience it will produce a severe lesion and may simulate an acute herpes keratoconjunctivitis.

With a fever like that from malaria, cortisone may be liberated from the adrenals in fairly large quantities. (See The Merck Report on *Action of Cortone*, 1951.) It is possible that this release of cortisone may be responsible for the development of herpes keratitis because it interferes with the fixed tissue immunity or with the nuclear membrane. Since fixed tissue immunity is so closely tied up with hypersensitivity, and cortisone affects the collagen response in hypersensitivity, then cortisone most likely prevents the aggressin from uniting with the virus.

Herpes-simplex infection may also be brought out by emotional disturbance, especially anxiety states. It is a well-known clinical observation that young people before an

* See van Rooyen and Rhodes, *Virus Diseases of Man*, page 167.

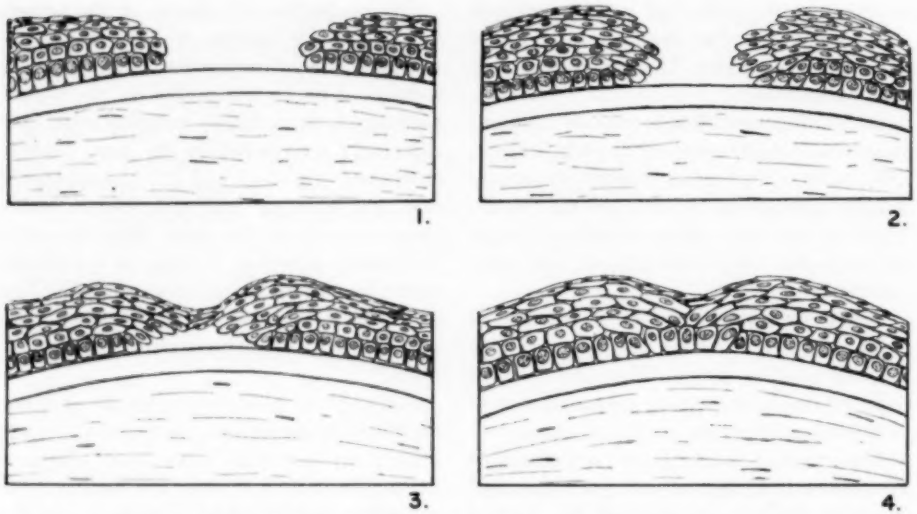

Fig. 3 (Braley). Healing epithelium of dendritic ulcer. (1) Ulcer. (2) Healing begins from intermediate cells. (3) Intermediate cells spread, filling the gap, leaving a space. (4) Basal cells formed from intermediate cells.

important speech or date may develop herpes lesions. This may be caused by overstimulation of the adrenal, with subsequent release of cortisone.

Our serum antibody studies in recurrent dendritic ulcer are most interesting, and in many respects contradict the findings of Burnet.[9]

We were fortunate enough to get blood from a young physician a number of years ago in doing a population study against another virus (epidemic keratoconjunctivitis). She completely neutralized the herpes virus through 10^{-1} dilution. She later developed a dendritic ulcer and, during the attack, her serum antibodies decreased to the point where she neutralized only the 10^{-3} dilution of virus. Her serum antibodies gradually returned to the previous high level as she recovered from the attack, and at the end of 30 days her serum antibodies were as high as on the first examination.

Recently we have tried to associate the circulating antibody titers with the attacks of keratitis. We have taken samples from 20 individuals with various stages of infection. A few days after the ulcer starts their antibodies are low and will neutralize 10^{-3}. When the disease is 14 days old, they neutralize 10^{-2}, and in 30 to 60 days their sera neutralizes up to 10^{-1}.

From these studies it would appear that the circulating antibody may also play some role in the healing of the corneal herpes.

Disciform keratitis associated with herpes

Occasionally, during an attack of herpes corneae, edema of the corneal stroma and wrinkling of Descemet's membrane occur. This usually develops on the seventh to 10th day of the disease, and while the epithelium shows signs of progressive healing, the edema of the cornea increases, and there develops a round opacity in the corneal stroma. This opacity is ordinarily grayish white, may be round or irregular in shape, as is illustrated in Figure 3.

The mechanism for the development of the disciform keratitis is not too well understood. It is, however, a type of collagen reaction similar to the reaction that is produced in the

cornea with scrofula, acne rosacea, and occasionally in phlyctenular disease of the cornea.

The disciform of herpes, however, is usually quite characteristic. After the disciform develops and the edema of the cornea begins to subside, then there are a good many deposits on the posterior surface of the cornea, and there is a mild to severe iridocyclitis.

I believe that this represents a hypersensitivity to herpes, and that the herpes virus, acting as an antigen, combines with the local and circulating antibodies to produce a hypersensitivity reaction. This hypersensitivity reaction is manifest first by the edema and then by the development of the disciform, and later the deep vascularization of the cornea. The evidence of hypersensitivity and hyperimmunity is borne out by some experimental evidence.

Hyperimmunity to herpes virus has been demonstrated repeatedly by many authors.* These authors have demonstrated that rabbits can be hyperimmunized to the herpes virus so that they produce immune bodies out of proportion to the amount of injected antigen.

There is very little evidence at the present time that there is an increase in the number of local immunization substancs, but from some of the work that we have been doing, rabbit's cornea can be made to produce what seems to be high titers of neutralizing substances.

A disciform keratitis may develop in any of the types of herpes. An individual may have repeated attacks of herpes corneae without producing any severe corneal damage, and then with a subsequent attack may develop a very severe disciform and uveitis. In the past it has been felt that the virus has been driven into the stroma and iris either by treatment or due to the lack of immunization substances.

Clinical experience, however, has shown that cortisone is very effective in treatment and prevention of the development of disciform. Cortisone may be applied locally to the eye when the disciform begins to develop. The edema will absorb while the eye remains clear without developing vascularization or severe scar. The corneal ulcer may continue to improve even under cortisone; either heal or become chronic. This would indicate to me that the herpes virus then produces a hypersensitivity of the cornea which in turn produces the typical hypersensitivity reaction in the cornea and uveal tissue.

Antibody studies of herpes cases that develop disciform are also very interesting. Their blood serum shows a slight drop in antibody titer during the first few days of the disease, but then there is usually a sharp rise in the antibodies so that a hyperimmunity state seems to exist. Their sera neutralizes in all dilutions of the virus, even through 10^{-1}.

Keratitis metaherpetica

Under ordinary circumstances, a herpes lesion runs its course and heals. In between attacks of herpes corneae, the cornea looks perfectly normal. There is no disturbance in the epithelium, although there may be a slight grayish infiltrate in Bowman's membrane beneath the site of the previous epithelial infection.

Under certain circumstances a herpes lesion tends to become chronic. This produces a roughening of the corneal epithelium with or without an associated disciform keratitis. The entire zone around the previous dendritic ulcer shows a marked variation in the thickness of the epithelium. At times there are multiple small bullae in the epithelium so that it may closely simulate a bullous keratitis.

There are, however, many areas in which the epithelium is absent, and these areas stain with fluorescein. The eye is irritable and there is a low-grade iridocyclitis. The epithelium does not cling to Bowman's membrane.

* See van Rooyen and Rhodes, *Virus Diseases of Man*, page 163.

This chronic phase of herpes may go on for months before permanent healing occurs. There may be small, recurrent dendritic ulcers or there may be only a superficial epithelial keratitis. This type of lesion is brought about by the failure of the epithelial cells to produce the basal layer of cells.

As you can see from Figure 3, it is the second and third layers of cells in the epithelium that fill in the defect produced by the ulcer. These epithelial cells spread in a syncytiumlike manner, spreading over the defect and multiplying as they spread. The second and third layers of cells are the most active ameboid cells. They are the large polygonal-shaped cells with a pale-staining cytoplasm and pale nuclei.

These cells also phagocytose any free virus that may be present, and tend to fix the virus in their nuclei. Under ordinary circumstances as they heal across the defect they form the basal epithelium. The basal layers of epithelium take considerable time to form, while the active ameboid cells may cover a defect in the cornea in a matter of a few hours.

In keratitis metaherpetica, a certain amount of fluid collects between these large polygonal-shaped cells and Bowman's membrane. Bowman's membrane may be slightly infiltrated with round cells, mostly lymphocytes and polys, and because of the presence of certain substances in the epithelium or Bowman's membrane (possibly aggressin), no basal cells are formed. This syncytium of superficial cells then proliferates, forming the flat surface cells of the cornea in great numbers. Consequently, the epithelium may thicken over the area where the fluid is present, but there is no attempt to form the basal cells of the epithelium.

By this means a chronic type of infection is produced, one in which there is a good deal of dormant virus present in the cells. But because of the overgrowth of epithelium and the excess fluid (globulin), a bullous keratitis is the result.

The scrapings are obtained from these corneas and smeared on a slide. The slide is so prepared that many of the epithelial cells are broken. Under these conditions it is possible to find the intranuclear inclusions in the broken nuclei of these large polygonal-shaped cells (fig. 2-3).

In order to develop the metaherpetic type of lesion, it is apparent that there must be a good deal of dormant virus present in the corneal epithelium. The virus is being constantly released, producing a mild inflammation that will be only partially neutralized by the surrounding neutralizing substances.

It is possible that the collections of fluid forming the bullae above Bowman's membrane are very high in local or circulating antibody. Since this fluid is rich in protein, which precipitates like globulin instead of like albumin, it may be formed from the gamma globulin fraction of the serum, in which case it would undoubtedly contain the antibody.

Keratitis metaherpetica then may also be a hyperimmune state much like the disciform type of keratitis, but that the immunity is largely derived from the blood serum instead of from the local fixed tissue histocytes as it is in disciform keratitis.

In the treatment of keratitis metaherpetica, the interference phenomena may be of some value. The interference phenomena is used in some virus diseases as a method of therapy.

By the interference phenomena we mean that, when one virus is present in a cell, the addition of another virus may replace the first virus and interfere with the growth of the virus in the cell. The interference phenomena is, however, not well understood and, although it is supposed that the addition of a new virus will replace the virus, there are a number of other possible explanations.

Repeated vaccination with vaccinia virus is the most prevalent means of utilizing the interference phenomena. The vaccinia virus, although it produces a cytoplasmic inclusion in the cell, may also stimulate the production of circulating antibodies.

I feel that the most likely reason for success of repeated vaccination with vaccinia

virus is that the gamma globulin fraction of the serum is increased and many antibodies are produced not only to vaccinia virus but also to the herpes virus, since nearly all of the antibodies are developed.

A new virus infection will increase the antibodies to a latent virus. Increasing the amount of antibody above the potency of virus will eventually keep the virus within the cell and not allow it to escape. If the virus does escape, then it is immediately neutralized by the existing antibodies.

Keratitis metaherpetica, therefore, represents a chronic type of herpes-simplex infection in which the local immune substances do not neutralize the virus. There is an overgrowth of epithelium which fails to produce basal cells.

The isolation of the virus from keratitis metaherpetica may be quite difficult. When the rabbit's cornea is inoculated by scrapings from the corneal epithelium of the patient, the transfer of the virus is not sufficient to produce an infection. We have been successful in isolating the virus on three occasions from the chronic type of herpes.

Using tissue culture methods of isolation, the virus must be passed by intracerebral inoculations in mice and back through tissue culture in order to increase its potency. On one occasion we were never able to increase the titer of the virus beyond 10^{-2} dilution. We have postulated that the amount of antibody carried with the virus is frequently sufficient to prevent the development of a highly potent virus. At the present time we are working on substances to remove the factors from the tissue culture that prevent the development of a potent strain of virus from metaherpetica.

Strain differences of herpes

There appears to be considerable difference in the manner in which herpes-simplex virus grows in tissue culture. Some strains of herpes virus transferred from tissue culture intracerebrally into mice have an incubation period of four to seven days before they will develop a typical mouse herpes encephalitis, while in other strains the mouse incubation period is uniformly three days.

This difference in incubation period does not appear to be a function of the virulence of the virus. If the incubation period is three days, the virulence of the virus will usually be about 10^{-3}. While those viruses with longer incubation periods may be slightly less virulent, they will kill mice through 10^{-3}.

Other types of variation may be found in the virus. One strain of herpes virus that we have always produces encephalitis in rabbits following corneal inoculation. The rabbits uniformly die in seven days. Another strain of virus produces the typical corneal lesions, but does not always produce the encephalitis in rabbits. One strain which we isolated from a case of metaherpetica remained only slightly virulent, even after many passages through mouse brain.

This variation is also seen in the susceptibility of herpes to aureomycin. Some strains of herpes virus are extremely susceptible to aureomycin, while other strains show no effect from aureomycin.

Immunologically, there does not appear to be any difference in the various strains of herpes virus. Individuals who have antibodies to herpes, whether these antibodies are produced by corneal lesion, by herpes labialis, or by herpes-simplex dermatitis all show the same type of antibody titers and all strains of virus are neutralized by all sera that have been tested.

In developing hyperimmunity serum in rabbits, however, there appears to be some slight strain difference. When hyperimmunity sera is developed to one strain of herpes virus, there will be more antibodies to the immunizing virus, while not quite as many when tested with other strains of virus.

Testing antiviral substances*

We became interested in studying the herpes-simplex virus when a number of

*R. C. Alexander, M.A., is co-author of this section of the paper.

clinical reports were made showing that aureomycin had some effect on the clinical lesions. We[15] reported that aureomycin solution applied in the eye healed some cases of dendritic keratitis. This finding was confirmed by Thygeson and several others. There was considerable controversy regarding the effect of aureomycin on herpes infection. Many observers have not found that aureomycin affected the course of the clinical disease.[16]

There is, however, little doubt that, if the herpes virus is mixed with aureomycin solution, the virus becomes noninfectious to rabbits' corneas and intracerebrally in mice. There is a wide variation of strains of herpes virus, and from our experiments and those of Thygeson, Gundersen, and Guyton, some strains are susceptible while others are not affected.[16]

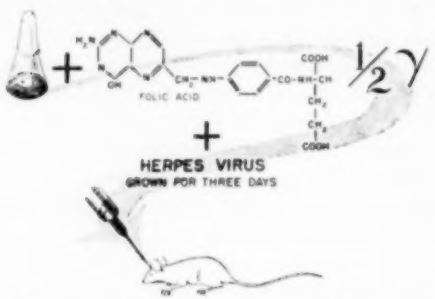

Fig. 4 (Braley). Tissue culture and folic acid with herpes virus inoculated intracerebrally into mice.

Since the crude aureomycin seemed to be more effective in treatment than the refined antibiotic, it would appear that something had been removed. One of the best methods of study seemed to be adding substances to tissue cultures used for growing herpes virus. We have found that a fairly standard concentration of herpes virus can be cultivated in fluid tissue culture. There were several substances in the crude aureomycin, so we started a systematic study of these substances. One of the first substances studied was folic acid.

Folic acid added to tissue culture inhibited the growth of the virus (fig. 4). One to two micrograms gamma did not affect the growth of herpes virus. (Herpes virus in

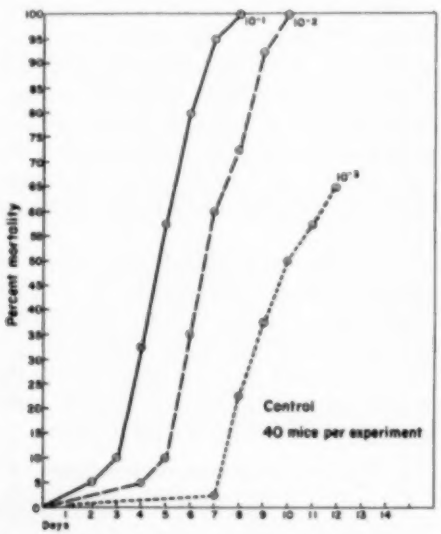

Fig. 5 (Braley). Growth of herpes virus in tissue culture. Mortality of mice after intracerebral inoculation.

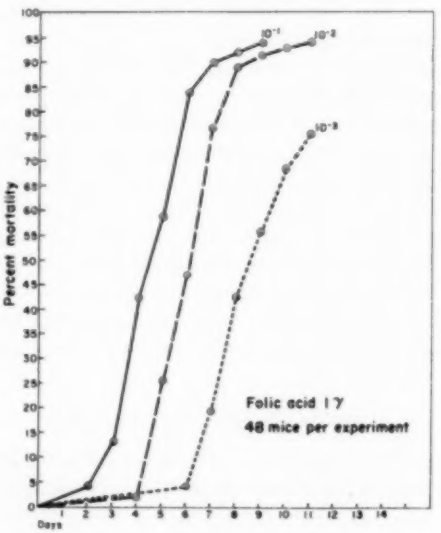

Fig. 6 (Braley). Folic acid, one gamma, added to tissue culture with virus, then tested intracerebrally in mice.

tissue culture is tested by intracerebral inoculation in mice.) From our tissue culture and our strain of virus, all mice are killed in 10^{-1} and 10^{-2} dilution, while 50 percent to 65 percent of mice are killed in 10^{-3} (fig. 5—control).

When folic acid is added to tissue culture in higher concentration of four to 30 γ per cc., there is a marked depression in the growth of herpes virus in the culture (figs. 6, 7, 8, 9, and 10). From these studies, it was concluded that folic acid inhibited the growth of herpes virus.

When folic acid was given to mice in protective tests, there was no protection against the virus. This led us to investigate how folic acid acted in our tissue culture. The standard tissue culture was made and allowed to grow for from three to five days.

The tissue was settled out by slow centrifugation and the tissue removed with a small amount of fluid. This was placed in the Warburg apparatus to measure the 0_2 consumption (fig. 11). The normal 0_2 uptake of the tissue from our cultures follows a straight line.

If folic acid is added in less than 1.0 γ per cc., there is definite depression in the 0_2 uptake. If folic acid is added in higher concentration, respiration can be stopped. When

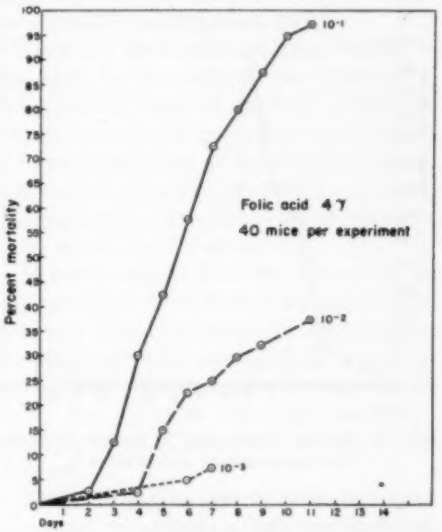

Fig. 8 (Braley). Folic acid, four gamma, in tissue culture, as in Figure 5. Note decreased potency to virus.

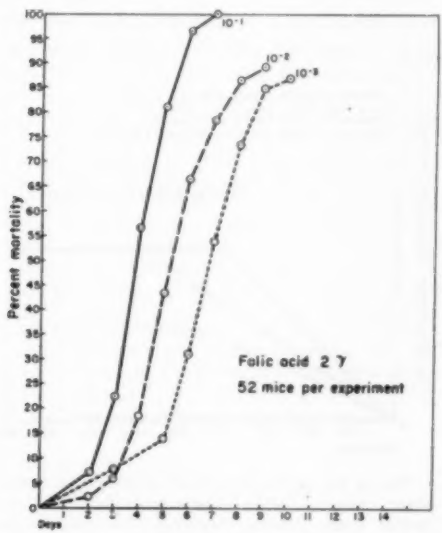

Fig. 7 (Braley). Folic acid, two gamma, added to tissue culture, as in Figure 5.

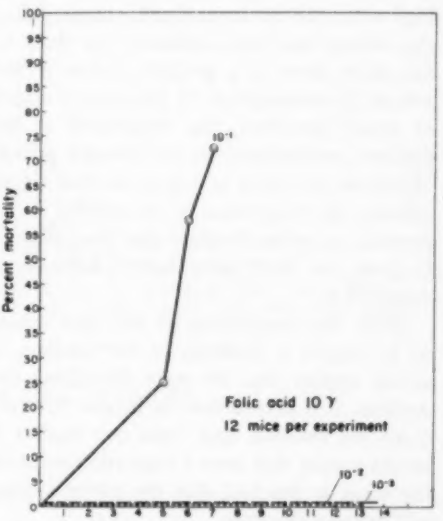

Fig. 9 (Braley). Folic acid, 10 gamma, in tissue culture with herpes virus, as in Figure 5. No deaths in 10^{-2} and 10^{-3} dilution.

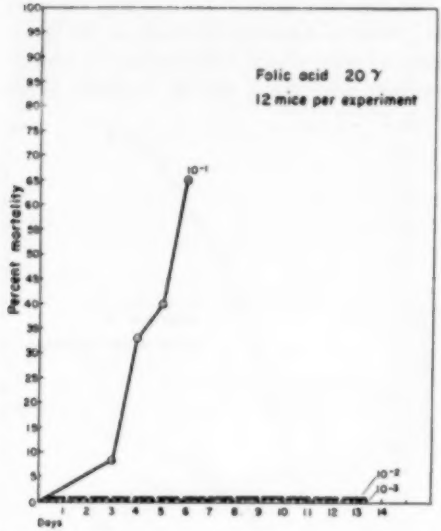

Fig. 10 (Braley). Folic acid, 20 gamma, to herpes virus tissue culture, as in Figure 5.

herpes virus is grown in tissue culture, it also depresses the 0_2 uptake.

We have studied the oxygen consumption of normal fluid tissue culture and have found that the rate of oxygen consumption is very high when the culture is freshly made. After the culture has been incubated for three to five days, there is a gradual decline in the rate of 0_2 consumption. If folic acid is added in small quantities, the respiration is depressed proportional to the amount added. When herpes virus is grown in fluid tissue culture, the respiration of the culture is depressed and after the virus has been allowed to grow for three days, there is little or no respiration.

Since the respiration of the cells seems to be largely a function of the nucleus, it would appear that we were disturbing the nucleus. It is known that the herpes virus attacks the nucleus, and from our studies it would appear that once a saturation point of the virus is reached, that the entire system will become dormant.

From our studies, we are unable to increase the virus potency of our tissue cultures beyond 10^{-3}. Likewise, when this point is reached, there is no further measurable respiration of the tissue culture. The cultures, however, when inoculated intercerebrally into mice show a high degree of potency of herpes virus.

When folic acid is added to tissue culture in small quantities, this material must depress or fix the nuclei in a dormant position in direct proportion to the amount of folic acid and the number of nuclei present. The folic acid must combine with the ribonucleic acid to form a stable substance which is now rendered impervious to the herpes virus. The herpes virus will quickly die if present in tissue cultures without ribonucleic acid.

Thus we concluded that folic acid acted on the nuclei of certain cells, rendering them inactive. This may help in explaining many of the confusing findings regarding the clinical use of folic acid for the anemias.

We can also explain our findings of the action of folic acid on the herpes virus. It is impossible to give enough folic acid to mice in a protective test to prevent infection with the herpes virus. Once the herpes virus is in the nucleus of cells, folic acid has very little ribonucleic acid to combine with and,

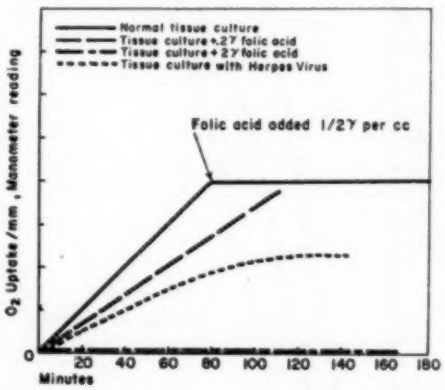

Fig. 11 (Braley). Oxygen consumption of normal tissue culture. Tissue culture with folic acid and herpes virus, showing depression in oxygen consumption. Note the decrease in oxygen consumption as the herpes virus grows.

therefore, would be useless in treatment of the disease.

Since folic acid showed these effects, it was natural for us to try many of the folic-acid antagonists. These included 4-amino pteroxylglutamic acid, 4-amino N^{10}-methyl pteroxylglutamic acid, 4-amino pteroxylaspartic acid, and pteroxyltriglutamic acid. None of these substances showed any effect on the herpes virus when tested in mice or clinical cases. They show, however, strange reactions when studied in tissue cultures.

Summary

Herpes virus is capable of producing various lesions in the eye. It produces an acute keratoconjunctivitis, dendritic ulcers, disciform keratitis, and a chronic bullous keratitis.

Acute keratoconjunctivitis is produced by the herpes virus as a primary infection. It occurs in individuals who have never had the disease prior to this infection.

Dendritic ulcer is a recurrent infection of the cornea in an individual who carries the virus as a latent infection. External and internal stimuli may change this latent virus into an active lesion.

Disciform keratitis is produced by herpes virus hypersensitivity.

Keratitis metaherpetica is a chronic herpes simplex virus infection associated with hyperimmunity and hypersensitivity.

There are local and circulating antibodies developed by the body to the virus which vary with the stage of infection. Hypersensitivity and hyperimmunity may be produced.

Strain differences of the virus are found, but human antibodies seem to be identical. The antibody is present in the gamma globulin fraction of the serum.

In tissue cultures the virus grows until all cell nuclei are filled with virus and then the cells and virus lie dormant. If the cell nuclei are combined with enough folic acid, it is not possible to infect the cells with herpes virus. Folic acid or folic-acid antagonists have no value in treatment of the clinical diseases.

Cortisone apparently releases the virus from the nuclei and spreads the infection. Cortisone, however, blocks the local hypersensitivity.

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16. Discussion in[15].

THE RELATIONSHIP OF RETINAL AND RENAL ARTERIOLOSCLEROSIS IN LIVING PATIENTS WITH ESSENTIAL HYPERTENSION*

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INTRODUCTION

For almost a century, the etiology and significance of the retinal changes in various cardiovascular-renal diseases has been of interest not only to ophthalmologists but to physicians in every field of medicine. It has long been recognized that the kidneys and eyes were often affected simultaneously by disease processes.

Controversy originally existed as to whether the retinal lesions were related to retention of nitrogenous waste products or were the result of retinal vascular disease. Some,[1,2] including von Graefe,[3] held the former view. Others,[4,5] including Gunn,[6] defended the latter view.

Beginning with Volhard,[7] present-day ophthalmologic thought has held that most of the retinal changes in various forms of kidney disease are due to retinal vascular disease. In essential hypertension all of the retinal changes are probably the result of retinal vascular disease. The underlying etiology of the retinal vascular disease, of course, bears a close relationship with the problem of the etiology of essential hypertension.

As a result of the brilliant researches of Goldblatt[8] in 1934, it was discovered that in the experimental animal renal ischemia could produce arterial hypertension. Since that time it has been agreed by most investigators that in the human certain forms of renal disease (glomerulonephritis and polycystic kidneys, for example) cause hypertension through some, as yet little understood, humoral mechanism.

Concerning the essential type of hypertension there has been a considerable difference of opinion. Goldblatt[9,10] has steadfastly maintained that persistent hypertension of the essential type is due to renal vascular disease, most usually to arteriolosclerosis but occasionally to sclerosis or other disease of the large vessels of the kidney.

The majority of investigators, however, hold that renal arteriolosclerosis is in most cases not the cause of this type of hypertension but an independent process enhanced by the hypertension, and at times aggravating the hypertension.

Bell,[11] Kimmelstiel and Wilson,[12] and Evelyn,[13] share this view. Castleman and Smithwick,[14,15] in a study of biopsy material from the kidney, concluded that renal arteriolosclerosis is not the cause of many cases of essential hypertension. It is felt the present paper will add additional evidence concerning the role of renal arteriolosclerosis in the etiology of essential hypertension.

Another question of perennial interest to ophthalmologists and others is the degree of correlation between the retinal findings and the findings elsewhere in the body in essential hypertension. Wagener and Kieth[16] found in muscle biopsies obtained from hypertensive patients that the severity of the changes in the arterioles of muscle and retina correlated quite well.

Many studies of vessels in the various organs have been made from autopsy material, but most of these studies did not include a study of the eye vessels and none correlated eye-vessel changes with changes elsewhere in the body. For a review of these the reader is referred to Farber and associates.[17]

Castleman and Smithwick[14,15] compared renal arteriolosclerosis to fundus changes in patients subjected to sympathectomy but did not compare renal with retinal arteriolosclerosis. They were attempting to correlate unlike changes in that the grading of their retinal changes (graded from normal through grade 4) was not based solely upon retinal arteri-

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olosclerosis but upon other alterations also, such as hemorrhages and exudates and papilledema.

To be valid, I feel that a comparison of retinal changes with kidney arteriolosclerosis should rest upon a grading in the eye based solely upon the degree of retinal arterioloclerosis. Since arteriolosclerosis is the primary organic lesion of essential hypertension, a correlation of this nature should tell us to what respective degrees the retina and the kidney participate in the disease process. It is felt that this study sheds light upon this question. Considering the frequency of use of the ophthalmoscope as an aid in the evaluation of the general condition of the patient with systemic hypertension, it is surprising that more studies have not been carried out.

Method

Patients who were to have sympathectomy had their fundi examined and the degree of sclerosis of their retinal arterioles was graded. The grading scale ranged from zero through four. *Zero grade* referred to arterioles showing no sclerosis. *Grades 1 to 4* were based upon the classification of the Committee on Classification of Hypertensive Disease of the Retina of the American Ophthalmological Society.[18] It is felt that this is the most accurate and most applicable method yet devised for the grading of generalized sclerosis of the retinal arterioles.

At the time of sympathectomy a kidney biopsy was taken. These biopsies average 0.5 by 0.5 by 1.0 cm. in size. The pathologist then graded the severity of the arteriolosclerotic process in the kidney on the same scale basis of zero through four grades. He was unaware of the eye grading. The basis of the pathologist's grading was that given by Bell.[11]

Eighty patients were examined; 26 were men and 54 were women. Their average age was 42.5 years. The blood-pressure readings ranged from 150/100 to 270/160 mm. Hg, with the average blood pressure 206/127 mm. Hg.

Results

The results are shown in Table 1 and summarized in Table 2. It will be noted that 86 percent of the cases showed a degree of sclerosis in the retina and kidneys either of the same degree or differing by not more than one grade. Figure 1 shows the frequency distribution of the various grades of sclerosis in the kidney and the eyes. There were no cases which showed grade four sclerosis in either the eyes or the kidneys.

Discussion

The method might be criticized from two standpoints.

First, it might be said that it is not valid to compare sclerosis of vessels observed microscopically with sclerosis observed ophthalmoscopically. However, it has been found that what we call sclerosis ophthalmoscopically is sclerosis pathologically and that the degree of sclerosis observed with the oph-

TABLE 1

Results of grading of sclerosis of retinal and renal arterioles

KIDNEY \ RETINA	Grade	0	I	II	III	IV	Totals
	0	4	11	8	—	—	23
	I	—	14	10	3	—	27
	II	—	12	13	1	—	26
	III	—	—	1	3	—	4
	IV	—	—	—	—	—	—
	Totals	4	37	32	7	—	80

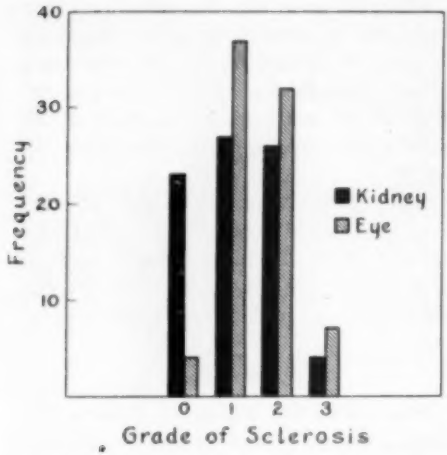

Fig. 1 (Wendland). Graph showing the distribution of the various grades of arteriolosclerosis in both the kidney and the retina. Frequency is expressed in actual number of cases.

thalmoscope corresponds to the degree observed with the microscope.[19, 20]

Even more important than this in answering this possible criticism is the fact that both the eyes and the kidney were graded on the basis of the same number of grades ranging from grade zero or normal vessels through grade four respresenting the most severe changes possible. We must, of course, always realize that nature does not draw sharp dividing lines and that in borderline cases the subjective interpretation of the observer must enter the picture.

Secondly, Goldblatt[9] has objected to the kidney biopsy method on the premise that it does not furnish an adequate sample of the kidney. However, Castleman and Smithwick[15] demonstrate that the kidney biopsy method is reliable in that each section contains about 50 cross-sections of arterioles and small arteries and, in a series of 100 cases in which bilateral renal biopsies were done, in 95 percent the grade in the two kidneys did not differ by more than one. Likewise as the sclerosis in the kidney became more severe as judged by biopsy, kidney function was progressively reduced.

It thus seems that biopsy of the kidney is a reliable method of determining the degree of renal arteriolosclerosis. The biopsy method does not determine the state of the larger renal vessels, of course, but it does determine the state of vessels comparable in size to the retinal arterioles.

Statistical analysis of our data in Tables 1 and 2 reveals that the probability the degree of association evident in the tables would arise through chance is less than three percent. Accepted statistical practice would, therefore, deem the data significantly demonstrative of direct correlation between the retinal arteriolosclerosis and that occurring in the kidney.

This association indicates that, in essential hypertension, the retinal arteriolar changes tend either to parallel or be somewhat more severe than similar changes in the kidney. The disease may proceed with some variability, however, and in the individual case one cannot say with certainty that the kidney changes are less severe than the retinal changes.

Statistically, however, there is an 84-per-

TABLE 2

SUMMARY OF RESULTS SHOWN IN TABLE 1

Total number of kidneys and retinas examined	80	
Number of kidneys and retinas of the same grade	34	69 (86%)—the number of eyes and kidneys either the same or differing by not more than one grade
Number of retinas more advanced than kidneys but differing by only one grade	22	
Number of kidneys more advanced than retinas but differing by only one grade	13	
Number of retinas more advanced than kidneys and in which grade differs by more than one	11	
Number of kidneys more advanced than retinas and in which grade differs by more than one	0	
Number having no kidney change yet retinal arteriolosclerosis	19	

cent probability that the retinal sclerosis will either equal or exceed the degree of kidney sclerosis. The retinal findings are thus an aid in the evaluation of the renal vessels. Examination of the graph will show immediately that the distribution of retinal arteriolosclerosis is displaced, relative to that in the kidney, in the direction of greater retinal arteriolosclerosis. The application of statistical tests for homogeneity (x^2) shows this to be clearly significant ($P = 0.001$).

From Table 1 it will be noticed that 23 of the 80 patients showed no renal arteriolosclerosis. When one considers that 19 of these 23 patients with no renal arteriolosclerosis already had a hypertension of sufficient severity and duration to have organic changes in their retinal arterioles, it seems unwise to conclude, as Goldblatt[9, 10] does, that renal arteriolosclerosis is the usual cause of essential hypertension.

The results in the present investigation are much more in accord with the view that the arteriolosclerosis in the kidney is either the direct result of the hypertension or an independent process enhanced by the hypertension.

Since the biopsy method does not enable inspection of the larger renal vessels, it might be argued that, in those cases showing no renal arteriolosclerosis, the hypertension was on the basis of some pathologic change in the large renal arteries of sufficient degree to alter renal hemodynamics. After a comprehensive review of this aspect of the subject, Yuille[21] concludes that "the actual number of reported cases in which hypertension is associated with obstructive lesions of one or both main renal arteries in man is not large and in only a small percentage of these can a definite etiologic relationship be established between the vascular lesion and the elevation of blood pressure."

It is unlikely that large renal-vessel pathology initiates hypertension even in the minority of cases but from my studies such a possibility is not ruled out and a few cases of hypertension seem to be on this basis.

It is germane to compare the frequency of retinal arteriolosclerosis observed in our cases of essential hypertension with that observed by Graham in his study of glomerulonephritis. In Graham's material, of 39 cases (proved at necropsy) of glomerulonephritis with hypertension, only eight or 20 percent showed retinal arteriolosclerosis, although they did show the other arteriolar signs of hypertension, namely generalized narrowing and focal narrowing. In our series of essential hypertensives, 76 out of 80 or 95 percent showed some degree of retinal arteriolosclerosis.

It is well known that hypertension in glomerulonephritis is often a terminal event. These findings thus corroborate the common belief that at least one of the factors that determine sclerosis of the retinal arterioles is the duration of the hypertension. Patients with glomerulonephritis and hypertension simply do not live long enough to develop retinal arteriolosclerosis.

These findings also may be of aid in an occasional case of hypertension in the differential diagnosis between glomerulonephritis with hypertension and primary hypertension. If the hypertensive patient presents much reduced kidney function and little or no sclerosis of his retinal arterioles, the case is probably one of glomerulonephritis. This observation is in agreement with Wagener.[22] If the eyeground sclerosis is severe and kidney function good, the case is very likely one of primary hypertension.

Summary

Eighty patients with essential hypertension, who underwent sympathectomy, had the retinal and renal arterioles examined and graded according to the severity of arteriolosclerosis present. Eighty-six percent of the patients showed sclerosis either equal in degree or not differing by more than one grade in the eyes and kidneys. Statistical analysis showed retinal sclerosis either to parallel or to be somewhat more severe than the kidney sclerosis. The retinal findings are thus an aid in the evaluation of the renal vessels.

Twenty-three patients showed no renal ar-

teriolar change but, of these, 19 showed retinal sclerosis. The results of the present investigation are in accord with the view that renal arteriolosclerosis is either the direct result of the hypertension or an independent process enhanced by the hypertension. The theory that renal arteriolosclerosis plays a frequent role in the cause of essential hypertension through alteration of renal hemodynamics and liberation of a pressor substance is not substantiated by the findings.

The difference in the frequency of retinal arteriolosclerosis in primary hypertension and in glomerulonephritis with hypertension is emphasized and the significance of this difference is noted.

The University of Minnesota Medical School (14).

Sincere appreciation is expressed to Dr. William T. Peyton and Dr. Lyle A. French of the Department of Neurosurgery for their coöperation in obtaining the kidney biopsies in this series.

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ON THE CHARACTER AND MANAGEMENT OF CIRCULATORY DISTURBANCES OF THE CENTRAL RETINA*

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INTRODUCTION

Presented herewith are 23 case reports of a variety of vascular disturbances of the macular region of the retina. Many names have been applied in the literature to this group of conditions in its various manifestations, such as central choroidal sclerosis, circinate retinitis, senile macular degeneration, macular edema, cyst of the macula, Kuhnt-Junius disease, central angiospastic retinopathy, and so on.

Most textbooks treat these conditions as separate entities. By these case reports it is intended to demonstrate how closely they are interrelated and that, contrary to the classical belief, they frequently respond to treatment. Therapy to be successful must have a rational basis and include an assessment and treatment of aberrations in the emotional status.

It is not the purpose of this article to discuss at any great length the pathologic changes that occur in these conditions. The literature on this subject, and also on the clinical aspects, is exceedingly wide.

An admirable review of these aspects has been presented by Benedict and Wagener[1] and by Duke-Elder.[2] Excellent discussions of the underlying vascular physiology of these conditions have been given by Gifford and Marquardt,[3] Duggan,[4] and Gifford.[5]

Suffice it to say that disturbances of the choroidal circulation lead to edema of the outer retina and, if severe or prolonged, to degeneration of those layers with migration of pigment from the pigment epithelium into the retina. Very acute disturbances may lead to hemorrhages in the choriocapillaris which then may track through to the retina.

On the other hand disturbances of the retinal circulation lead to edema and even hemorrhages or exudation in the inner retina. On subsidence these latter are much more likely to lead to restitution to integrity than do dysfunctions of the choroidal circulation.

CIRCULATION OF MACULA

In reviewing the literature dealing with the circulation of the macula, it is clear that this region is particularly vulnerable to vascular disturbances. Some explanation for this can be deduced from histologic studies which indicate that the nutrition obtained from the choroidal circulation is ample, or at least as ample as that of the rest of the retina. As Duke Elder,[6] among many others, has pointed out, however, the fovea and immediate vicinity is entirely avascular. Surrounding this area there are numerous capillaries supplied by arterioles some distance away. This latter would appear to be a vulnerable arrangement in itself.

Since an abundant retinal vascular pattern in this area would interfere with the perception of light, it is at a minimum. At the same time the nutritional requirements of the macular region are relatively high compared to the rest of the retina, owing to the density of the neuronal elements.

It is obvious then that the nutritional reserve in this area must be relatively small and that even the smallest reduction of the minute volume of the arterial flow will have a severe effect. Hence, circulatory disturbances that might well be tolerated elsewhere without loss of function may be expected rapidly to produce changes in the macula.

In some cases, the disturbances that upset the nutrition of the macula may occur principally in the retinal circulation. In others, the changes may be mainly in the choroidal circulation. In still others, both circulatory regions may be involved.

As is well known, the commonest causes

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for slowing of the arteriolar circulation are arteriolar spasm and arteriolar sclerosis. They may act alone or together.

Depending upon which element plays the predominant role the picture will vary. An excellent histologic and clinical study of interplay of these two factors in the macular region has been published recently by Klien.[7]

Factors operating in circulatory disturbances

It is obvious then that there are at least four possible variables operating in this group of conditions: arteriolar spasm and arteriolar sclerosis, the choroidal and the retinal circulations. Depending upon the interplay between these four varying factors one may account for a large variety of different clinical pictures that one meets in the macular region.

These disturbances will range at one end from those which are due entirely to arteriolar spasm through that group in which both spasm and sclerosis play a part, to finally that group in which sclerosis plays the only part. In some patients the choroidal circulation may be mainly affected, in others the retinal circulation may be mainly affected, and in a third group the two may act together.

The intimate interrelationship of these features had been pointed out by many authors—Bailliart,[8,9] Cattaneo,[10] and Duggan.[4] As already mentioned, Klien[7] has provided histologic confirmation of these theories. Sorsby[11] and Pillat[12] have shown that there is a strong hereditary element in those cases in which the condition is due mainly to sclerosis of the choroid. The lesion then is usually bilateral.

Our knowledge regarding the cause of arteriolar sclerosis is poor. Consequently our means of controlling its development are extremely poor. However, considerably more is known of arteriolar spasm and the neural and hormonal pressor effects that bring it about.

Not least among these are the emotions which have been pointed out as possible causative factors in central angiospastic retinopathy by Horniker,[13] who first described the condition. An excellent study of this aspect of this disease has been published recently by Harrington.[14,15] He presents much data to support his view. Zeligs[16] also has made a study of the psychosomatic factors in central angiospastic retinopathy. He found anxiety was a common causative factor.

Treatment

Many textbooks present a defeatest attitude when discussing the treatment of this condition. In 1938, Zentmayer[17] expressed the traditional view, which still is held widely, when he said: "There are of course many other senile changes met with in the eye such as macular degenerations, but their early detection is not of great importance, as we can do nothing for them."

Duke-Elder[2] agrees in essence stating that: "The condition is due essentially to processes outside medical control."

Duggan,[4] however, felt that not only were all these senile changes interrelated but that they very frequently could be treated successfully with vasodilators.

Berens[18] also has taken a hopeful attitude and has expressed his opinion that attention to the general hygiene, rest, and the reduction of excesses in alcohol and tobacco have an ameliorating effect. He also feels that vasodilators have a wide use.

Influenced by these somewhat theoretical considerations all patients with these conditions have for some years been treated with vasodilators. An effort has been made to uncover and correct any anxieties. Also attention has been paid to the investigation and correction of disturbances in the general medical condition. Whenever found, foci of infection were eliminated.

Clinical studies

As part of this article are the condensed case histories of 23 consecutive patients with circulatory disturbances in the central retina. No selection of any sort has been carried out, save to exclude patients with malignant hy-

pertension, nephritis, or diabetes mellitus.

In similar studies by other authors usually all hypertensive patients have been excluded. Milder cases only have been included here as they seem to form a natural though borderline group. The essential findings of these case histories are presented in Table 1.

The cases are arranged in diagnostic groups which in turn are arranged in related sequence. With attention to the considerations already outlined, it is possibly significant that the patients fall naturally in these groups and the groups run smoothly one into another.

Conditions represented

The first three cases represent central choroidal sclerosis. In these there was little or no change in the retinal vessels, and the condition appeared to be due entirely to sclerosis of the choroidal vessels.

In one case only was there a definite anxiety factor. Possibly significantly this was the only one that showed any improvement with treatment. Since the condition is due mainly to arteriolar sclerosis, it is not surprising that it does not respond to any presently known therapy and that little response to vasodilators can be expected.

The next is a case of Tay's central choroiditis. Some may question the validity of incorporating such a one in this group. Bedell,[19] among many others, however, would include it. He feels it is a senile degeneration manifesting a circulatory disturbance. It is interesting to note that this patient's vision has deteriorated slowly in spite of treatment.

Case 5 is one that has features suggesting a mixture of both choroidal sclerosis and retinal circulatory changes. His disturbance began with macular edema and retinal hemorrhages and he was left with central retinal atrophy through which sclerosed choroidal vessels could be seen. Vasodilator therapy apparently has kept the condition in his other eye under control.

TABLE 1

Essential findings in the cases studied clinically

Case No.	Sex	Age	Blood Pressure	First Seen	Diagnosis	Anxiety Status	Vision		Course
							Before	After	
1	M	78	140/80	Mar./49	Central choroidal sclerosis	0	6/7, 6/240	6/240, 6/240	Worse
2	F	76	140/85	Sept./51	Central choroidal sclerosis	+++	6/9, 6/60	6/6, 6/60	Slightly better
3	F	87	155/85	Nov./51	Central choroidal sclerosis	0	6/20, 6/240	6/20, 6/240	Holding
4	F	87	140/80	Sept./46	Tay's choroiditis	0	6/12, 6/9	6/20, 6/30	Worse
5	M	79	135/80	Jan./49	Senile macular degeneration (borderline choroidal sclerosis)	0	6/24, 6/6	6/60, 6/7	Holding
6	F	60	140/95	Feb./49	Circinate retinitis	+	6/20, 6/60	6/20, 6/60	Holding
7	F	61	170/95	May/48	Macular degeneration, evanescent circinate retinitis, retinal arteriolar sclerosis and spasm	+++	6/6, 6/7	6/6, 6/240	Holding
8	F	51	145/80	Sept./51	Circinate retinitis (related to angiospasm)	+	6/15, 6/6	6/20, 6/6	Worse
9	M	57	115/70	Oct./51	Senile macular degeneration	+++	6/9, 6/12	6/60, 6/18	Worse
10	M	73	140/85	Sept./48	Senile macular degeneration	+++	6/6, 6/15	6/6, 6/9	Slightly better
11	M	77	130/85	Nov./51	Senile macular degeneration	0	6/15, 6/240	6/9, 6/240	Slightly better
12	F	72	150/84	Dec./51	Senile macular degeneration	++	6/9, 6/7	6/9, 6/7	Holding
13	F	72	180/95	June/49	Hypertensic., arteriolar sclerosis, senile macular degenefation	0	6/9, 6/60	6/9, 6/60	Holding
14	F	73	170/85	Apr./50	Hypertension, arteriolar sclerosis, senile macular degeneration	0	6/240, 6/240	6/240, 6/240	Holding
15	F	66	160/90	Feb./50	Hypertension, arteriolar sclerosis, senile macular degeneration	0	6/15, 6/9	6/20, 6/30	Worse
16	M	70	180/95	July/49	Aphakia, hypertension and arteriolar sclerosis, senile macular degeneration	+	6/12, 6/60	6/18, 6/60	Holding
17	F	64	170/95	Jan./50	Hypertension and arteriolar sclerosis, senile macular degeneration	+++	6/60, 6/240	6/7, 6/120	Better
18	M	26	120/75	June/44	Central angiospastic retinopathy, (Kuhnt-Junius Disease)	+++	6/6, 6/240	6/6, 6/240	Holding
19	F	55	135/75	Mar./48	Central angiospastic retinopathy	+++	6/240, 6/7, pt	6/240, 6/6	Holding
20	M	48	130/80	Feb./44	Central angiospastic retinopathy	++	6/6, 6/9	6/6, 6/240	Holding
21	F	51	120/70	Nov./49	Central angiospastic retinopathy	+++	6/120, 6/6	6/6, 6/6	Cured
22	M	45	130/75	May/43	Central angiospastic retinopathy	++	6/6, 6/18	6/6, 6/6	Cured
23	M	30	125/75	Mar./49	Central angiospastic retinopathy	+++	6/6, 6/60	6/6, 6/6	Cured

Cases 6, 7, and 8 were most interesting. The first was a typical example of retinitis circinata.

The second had retinitis circinata in one eye only and the exudate lasted only a few weeks at which time it was associated with gross spasm of the upper and lower temporal arterioles. In the other eye at no time was there any circinate exudate but from time to time there was macular edema. This patient had moderate hypertension and arteriolar sclerosis.

The third patient had no arteriolar sclerosis but mild hypertension and Raynaud's disease. Anxiety was a prominent feature in the second case.

The next four patients (Cases 9, 10, 11, 12) were typical examples of senile macular degeneration. Ophthalmoscopically there was mild arteriolar sclerosis but no evidence of arteriolar spasm and there was no hypertension. There was macular edema going on to degeneration. Anxiety was a feature in three of these cases. Treatment appeared at least to keep this group from getting worse.

The next five cases showed essentially the same condition but all these patients suffered from mild to moderate hypertension. In one patient the condition followed a cataract extraction. Two of the five patients had a marked anxiety status.

The next six patients (Cases 18, 19, 20, 21, 22, and 23) had what might be classified broadly as central angiospastic retinopathy. Some may deny the validity of including all these cases under such a heading. Gifford[3,5] felt that true central angiospastic retinopathy is due entirely to a disturbance of the retinal circulation.

In only three of the present cases does this condition pertain (Cases 21, 22, 23). In Case 20 both the choroidal and the retinal circulation were very evidently involved. In this same patient the two circulatory areas were affected separately at different times and on other occasions they were affected simultaneously.

Case 19 apparently represents a disturbance of the choroid, mainly of a spastic nature; while in Case 18, the disturbance must have been in the choroid and of a most acute nature, so that the picture of Kuhnt-Junius disease was produced.

In all this group there was a marked anxiety feature. Only Cases 21, 22, and 23 conform to Gifford's definition of the condition and in these only was recovery complete. Gifford[3,5] states that full recovery is a feature of central angiospastic retinopathy.

A study of the clinical findings of these 23 cases shows very clearly that it is a mistake to consider them as a group of entities. One clinical type merges into another as do the colors in the spectrum.

By the interplay of arteriospasm and sclerosis in the retinal and choroidal circulations all the clinical pictures described here can be accounted for, thus supporting the theories of Bailliart,[8,9] Cattaneo,[10] and Duggan.[4] Histologic confirmation of these theories has been presented by Klien.[7]

In many standard texts it is pointed out that treatment is unavailing in these conditions. But Gifford and Marquardt,[3,5] Duggan,[4] and Berens[18] have all pointed out that this is by no means the case. General improvement of the state of health, protection from cold and excessive use of tobacco and alcohol, increased rest, removal of foci of infection, and vasodilator drugs all have been used with success.

The present study upholds this point of view. As might be expected, treatment appeared to be most efficacious where there was little or no arteriolar sclerosis, and in the lower age groups.

In certain of the present group the correction of an anxiety status had a most important effect. By the word "anxiety" is meant the effect of emotional stress. None of the present patients could be considered to be suffering from anxiety neurosis. This etiologic factor though mentioned by many authors has not been emphasized.

It is clear from the present study that the psychic status cannot be ignored. Indeed, it

is so important that the psychiatrist, and even social services, should be called upon wherever indicated.

In the present series, anxiety was a marked feature in over one half of all the cases. It was most prominent in those patients in whom there was marked angiospasm. Close study of the clinical course of these cases shows that improvement was greatest where there was anxiety and where it could be controlled.

Serious consideration should be given to including many of these cases under the heading of psychosomatic disease. There is no doubt that this should be the case with central angiospastic retinopathy as already suggested by Harrington[14,15] and Zeligs.[16] But it is clear from the clinical course of the cases in this study that the same factor affects other vascular disturbances also.

It may be stated generally from this study that the efficacy of treatment was greatest and the prognosis best, the less marked was the element of arteriolar sclerosis, the younger the age, and the shorter the duration of the disease, and when angiospasm associated with anxiety was the main feature.

Summary and Conclusions

1. A study is presented of 23 consecutive cases of disease of the central retina related to disturbances of the retinal and choroidal circulations.

2. The ophthalmoscopic appearance and pathogenesis of these conditions can be accounted for on the basis of the interplay of four factors: arteriolar spasm and arteriolar sclerosis which affect the choroidal and retinal circulations either separately or together.

3. The present study indicates that these conditions, though traditionally considered entities, actually merge one into the other and form a group.

4. Emotional stress plays an important etiologic role.

5. Contrary to the traditional view, therapy is helpful. This should be rational and directed to reduction of the emotional stress and to producing vasodilatation.

6. In this study the efficacy of treatment was greatest and the prognosis best, the less marked was the element of arteriolar sclerosis, the younger the age, and the shorter the duration of the disease, and when angiospasm associated with anxiety appeared to be the most marked feature.

Case Reports

Case 1

F. G. A., a man, was seen first in March, 1949, at the age of 78 years.

The patient stated that the vision in the left eye always had been poor but during the previous five or six months it had become steadily worse. On examination vision was: R.E., 6/7; L.E., fingers at five feet.

The fundus examination showed marked tessellation of each retina. The right nervehead was normal but the left nervehead showed pallor on the temporal side. Both macular areas appeared normal.

The general state of health was good. The psychologic status was normal. The blood pressure was 140/80 mm. Hg.

During the next month, very fine pigmentation appeared in the left macular region, the right macula remained normal. In May, the vision was: R.E., 6/9; L.E., still fingers at five feet. The patient was placed on nicotine acid (50 mg., three times daily). The visual condition steadily deteriorated. The pigmented area in the left macula increased in degree and size.

By January, 1950, vision was: R.E., 6/18; L.E., still only fingers at five feet. By this time, a large pale area of retinal atrophy had appeared in the macular area of the left eye through which large sclerosed choroidal vessels could be seen, and now there was mild pigment stippling of the right macula. The condition in the right eye continued to develop until it was the same as that in the left. By January, 1951, the patient's vision was only fingers at five feet in each eye.

Diagnosis. Central choroidal sclerosis.

Case 2

H. F., a woman, was first seen on September 10, 1951, at the age of 76 years.

The patient complained that she had had blurred vision for the previous two or three months. The general health appeared to be good, although the patient stated that her memory had been poor for some time. The patient was a highly nervous, though not neurotic, individual and had suffered from migraine for years. She was terrified about becoming blind. A very close friend of hers had had severe eye trouble related to secondary glaucoma.

The examination showed that she had 6/9 vision, R.E., and 6/60, L.E. The fundi showed no disturb-

ance in the vessels, the arterioles were not constricted nor sclerosed. The right macula showed very mild pigment mottling, but the whole left macular region was markedly tessellated. The appearance of the left fundus was that of retinal degeneration associated with choroidal sclerosis.

The patient was placed on nicotinic acid (50 mg., three times daily). After two months, there was no improvement in the vision. The patient was then put on priscoline (25 mg., three times daily). She almost at once felt better. The vision improved to: R.E., 6/6, partial. There was no improvement in the vision of the left eye. There was no visible change in the fundi.

Medical examination disclosed no disturbance but early arteriosclerosis. The blood pressure was 140/85 mm. Hg.

Diagnosis. Central choroidal sclerosis.

CASE 3

R. S., a woman, was seen first in November, 1951, at the age of 87 years.

The patient was a very bright active individual for her age. She stated that, during the previous two or three years, she had had fainting spells on two or three occasions. On one occasion this was followed by weakness on one side, and probably represented a mild stroke. There was no evidence of any anxiety in her history. The patient was a well-adjusted individual.

For the previous eight months the patient had noticed failing vision in both eyes. On examination, vision was found to be: R.E., 6/20; L.E., 6/240. This could not be improved by correction. The fundi were similar. In the macular region of each eye the choroidal vessels could be well seen through a large patch of atrophied retina. In this area there was increased pigmentation and the choroidal vessels were sclerotic. The retinal vessels were of normal caliber and showed only the very mildest degree of arteriolar sclerosis. There were no hemorrhages or exudates and the nerveheads were normal.

A general medical examination was negative save for moderate arteriosclerosis. The blood pressure was 155/85 mm. Hg. The condition did not respond to any treatment.

Diagnosis. Central choroidal sclerosis.

CASE 4

C. E. H., a woman, was seen in September, 1946, at the age of 87 years.

The patient stated that she had had a slight loss of vision during the previous three or four years. The patient was an exceedingly well-preserved elderly lady in excellent health. She had no other complaints and no anxieties.

Examination showed that vision was: R.E., 6/12; L.E., 6/9. The fundi were essentially similar with generalized Grade-1 arteriolar sclerosis. There was no arteriolar spasm. The macular region of each eye showed numerous closely arranged pale areas like large drusen.

The general medical examination disclosed no disturbance aside from moderate arteriosclerosis. The blood pressure was 140/80 mm. Hg.

After the patient's first examination, there was a slight and gradual loss of vision, until now it is: R.E., 6/20; L.E., 6/30. There has been slight edema from time to time in the fovea region of one or either eye.

During the past six months the patient has been taking nicotinic acid (25 mg., three times daily before meals). On this treatment she has had subjective improvement. There has been little or no actual improvement of the visual acuity and no change in the fundus picture.

Diagnosis. Tay's choroiditis.

CASE 5

D. W. T., a man, was seen first in January, 1949, at the age of 79 years.

The patient stated that two weeks previous to his examination he had noticed blurring of the vision of the right eye which steadily had become worse. Examination showed that the vision was: R.E., 6/24; L.E., 6/6.

The fundus examination showed that the arterioles were not narrowed but that they were mildly sclerotic (grade 1). The macula of the left eye was quite normal. The macula of the right eye was quite edematous, showing mottled rarefied and pigmented areas. There were a few minute flame-shaped hemorrhages scattered over this area. Choroidal pigment (tessellation) was moderately prominent in each eye.

The patient was placed on rutin and nicotinic acid (50 mg., three times daily).

A complete medical examination disclosed no disturbance except for a mild degree of arteriosclerosis. The blood pressure was 135/80 mm. Hg.

In spite of treatment there was no improvement in vision. The visual acuity of the right eye did not improve, though the fundus picture became quieter, the edema disappeared leaving a large scarified area in the macular region. During this period a very mild pigment stippling of the left macular area appeared, but the vision remained at 6/7.

Since this time the patient has been maintained on nicotinic acid and rutin and there has been no further loss of sight in the left eye.

Diagnosis. Senile macular degeneration(borderline central choroidal sclerosis).

CASE 6

R. M. C., a woman, was seen first in February, 1949, at the age of 60 years.

The patient stated that following the death of her husband two years previously there had been a gradual loss of vision in each eye. At examination the vision was: R.E., 6/20; L.E., 6/60.

Examination of the fundi showed a well-developed circinate retinitis of each eye and marked macular edema. The retinal vessels showed moderate arteriolar sclerosis (grade 2). The caliber was normal.

A general medical examination disclosed nothing

of importance. The blood pressure was 140/95 mm. Hg.

The patient was placed on rutin and nicotinic acid which drugs have been continued at intervals since that time with no improvement in vision and no change in the fundi except for the gradual appearance of mottled rarefied and pigmented areas in each macula.

Diagnosis. Circinate retinitis.

CASE 7

H. R. C., a woman, was seen first in May, 1948, at the age of 61 years.

The patient complained that she had had a spot before the left eye for the previous three weeks. Vision (corrected) was: R.E., 6/6; L.E., 6/7.

Examination of the fundi showed a generalized Grade-1 to Grade-2 arteriolar sclerosis. The arterioles appeared of normal caliber. There were no hemorrhages or exudates. There was very faint edema of the left foveal region. The right foveal region was normal.

The patient was checked over completely and investigated for foci of infection but no abnormality was found save for mild hypertension. The blood pressure was 170/95 mm. Hg.

By October, the vision was: R.E., 6/6; L.E., 6/12. The left macular edema had become more pronounced. The patient was placed on rutin and nicotinic acid. The condition ceased to progress and the vision remained at this level until December, 1948.

The loss of vision in the first instance came on one month after the sudden death of her husband. Following this the patient had to take over the management of his firm. There were many associated worries and anxieties. There came a period of increased anxiety in January, 1949, and with this there was a sudden further loss of vision in the left eye.

When seen in January, vision was: R.E., 6/6; L.E., 6/400. Examination showed a large patch of intense edema of the left macula. There was marked spasm of the left superior and inferior temporal arterioles throughout their whole length (grade 2 to grade 3). There were no hemorrhages or exudates.

The patient was placed on rutin and nicotinic acid. The condition continued without improvement until April when there was a short period of slight improvement of the vision in the left eye.

By June the condition had again relapsed so that the vision was: R.E., 6/6; L.E., 6/240. Now over and above the previous findings in the left macular region, there was much waxy white exudate arranged in a circinate manner about the left macula. The rutin and nicotinic acid were continued.

By January, 1949, the vision had remained fixed at: R.E., 6/6; and L.E., 6/240. The left macula was much less edematous. There was still marked spasm of the upper and lower left temporal arterioles and much waxy white exudate arranged in a circinate manner.

By March, 1949, the vision had not improved but now there was less spasm of the arterioles of the left eye and there was less edema. In September, 1949, vision was: R.E., 6/6; L.E., 6/120. The waxy exudate in the left eye had disappeared and there was no evidence of circinate exudate or, indeed, of any exudate, and there was no evidence of arteriolar spasm. The retina in the left macular region had atrophied and showed considerable pigment mottling.

This improvement in the retinal picture in the left eye coincided with the settlement of her business affairs. In February, 1951, she had a slight exacerbation in the right eye. There was slight edema of the right macula and the vision fell to 6/9 (partial) in this eye, but there was no waxy exudate. This occurrence coincided with the serious illness of her daughter, during which time she carried out all the nursing duties.

The patient was placed again on rutin and nicotinic acid. This time the vision in the right eye improved to 6/6, but the left eye remained unchanged. The edema disappeared in the right macular region leaving a slight fine pigment mottling.

Diagnosis. (1) Macular degeneration related to evanescent circinate retinitis; (2) retinal arteriolar sclerosis and angiospasm.

CASE 8

M. N., a woman, was seen first in November, 1946, at the age of 51 years.

The patient first came for the prescription of reading glasses. She had 6/6 vision in each eye. The fundi were quite normal in all respects.

She was seen at intervals following this for the checking of her glasses. She returned in September, 1951, stating that the vision of the right eye had been blurred for about two weeks.

The patient always had been relatively healthy, although she states that she had been troubled with chilblains and with a mild Raynaud's disease for many years. She always had got easily chilled in the winter time. There never had been any tissue necrosis.

There was no marked emotional disturbance. The patient is the sole support of an invalid mother. She had just retired from school-teaching and was finding some difficulty in adjusting herself to her new way of life.

The examination in September, 1951, showed the vision was: R.E., 6/15, partial; L.E., 6/6. In the fundi the vessels were absolutely normal in all respects. The arterioles were not constricted nor were they sclerotic. The left foveal region was quite normal, but the right foveal region was mildly edematous. Arranged about the right macula in an imperfect crescent were conglomerations of punctate waxy-white exudate.

The patient was given a complete medical examination. No foci of infection were found and no vascular disease, aside from mild Raynaud's disease, was discovered. The blood pressure was 145/80 mm. Hg.

The patient was put on nicotinic acid (50 mg., three times daily). Following two months of this

treatment the blood pressure dropped to 136/80 mm. Hg., and remained there.

However, at her last examination, five months after the inception of her trouble, the vision of the right eye had dropped to 6/20. The left eye remained at 6/6. About the right macula the exudate had increased and just below the fovea was a small cystlike area.

Diagnosis. Circinate retinitis (related to angiospasm.

CASE 9

A. E. B., a man, was seen first in 1940, at the age of 47 years.

The patient had been seen at intervals for hypermetropic astigmatism since 1940. In March, 1950, at age of 57 years, with correction, he had 6/6 vision in each eye.

During the following summer he became aware of periods of slight blurring of the vision. However, this was not sufficiently bad for him to ask for an examination until October, 1951. At this time it was found that the best corrected vision of the right eye was 6/9 and of the left, 6/12.

The fundi showed quite a moderate degree of generalized arteriolar sclerosis. The arterioles showed Grade-2 generalized sclerosis, but there was no narrowing of the caliber. There were no hemorrhages or exudates. Each macula was edematous and showed mottled pigmented and rarefied areas.

As the patient was working under considerable pressure and had been for the previous year, he was advised to reduce his work and have a complete medical check-up.

The patient is a highly energetic and conscientious individual. Besides his work as a railroad permanent-way engineer, he also had undertaken the supervision of the building of a new church. This entailed a great deal of work as he was acting for an absentee architect. He also was very active as an executive of several committees in his community.

A general medical examination was essentially negative. The blood pressure was 115/70 mm. Hg.

The patient was seen again in November, 1951, at which time there had been a further decrease in vision: R.E., 6/60; L.E. 6/18. The fundi however were unchanged.

At this point the patient was advised to take a complete rest from all work. He gave up all duties in respect to his job and his various committees and remained at home. He was put on phenobarbital (0.25 gr., threee times daily) and priscoline (25 mg., four times daily).

Examination a month later showed that progress had ceased. By February, 1952, the vision was still: R.E., 6/60; L.E., 6/18. The maculas were still edematous and mottled, and now there was waxy exudate about each, appearing like an early circinate retinitis.

Diagnosis. Senile macular degeneration.

CASE 10

G. A. C., a man, was first seen in September, 1948, at the age of 73 years.

The patient was a highly nervous and excitable, though not a neurotic, person. He had noticed a failure of the vision in the left eye for about a year previous to his examination. The patient had been under great stress, owing to the serious illness of his wife. His wife, who had cancer of the bowel, was undergoing repeated operations.

Examination showed vision to be: R.E., 6/6; L.E., 6/15. The fundi showed mild arteriolar sclerosis throughout but no arteriolar spasm. There was marked edema of the left macular area, and very mild similar changes in the right eye.

The general medical examination disclosed no disease. The blood pressure was 140/85 mm. Hg.

The patient was placed on rutin and nicotinic acid. His vision improved slightly until February, 1949. At this time vision was: R.E., 6/6, L.E., 6/9. The fundus of the right eye was absolutely normal. That of the left eye showed slight pigment mottling of the foveal region.

There was a slight exacerbation in May, 1949, at which time his wife became seriously ill. But it rapidly quietened down. His wife died shortly after this and since then there has been no more trouble with his vision.

Diagnosis. Senile macular degeneration.

CASE 11

D. J. K., a man, was first seen in February, 1951, at the age of 77 years.

When first seen, the patient had full vision in each eye. He stated that he had been well continuously since that time until four weeks before examination in November, 1951, at which time his hands and feet began to swell. He also had fleeting stabbing pains in his fingers and some numbness in the third finger of the right hand. One week later he noticed difficulty in reading. This came on quite suddenly overnight. There was no evidence of any anxiety or nervous tension.

On examination, with correction his best vision was: R.E., 6/15, partial; L.E., 6/240. Fundus examination showed mild generalized arteriolar spasm (grade 1). There was generalized Grade-2 arteriolar sclerosis. The venules showed Grade-1 compression where crossed by the arterioles and were not engorged or tortuous. There were no hemorrhages or exudates.

The macula in the right eye showed mild diffuse edema with no disturbance of pigmentation, but that of the left eye showed mild edema with mottled pigmented and pale areas. The picture was that of senile macular degeneration.

Aside from the edema of the hands and feet, medical examination was essentially negative. There was moderate arteriosclerosis. His blood pressure was quite normal for his age at 130/85 mm. Hg. A possibly significant feature was that the patient had been troubled increasingly with the cold for the previous six months.

The patient was placed on priscoline (25 mgs., three times daily). Following two months on this therapy the patient stated that he was feeling much better generally. He was brighter and less easily chilled, and now he could read. Vision was: R.E., 6/9, partial; L.E., 6/240.

Diagnosis. Senile macular degeneration.

CASE 12

D. A. R., a woman, was first seen in December, 1951, at the age of 73 years.

The patient stated that she had a cloud before the center of the vision of the right eye. She also saw floating black objects before the right eye. However, the vision was not so bad that she could not read. The cloud was always present, and had been there for four weeks. Four weeks previously the patient moved her home from one building to another, this necessitated a great deal of work and anxiety on her part, as it represented a change of domicile after many years in one place.

Vision with glasses was: R.E., 6/9; L.E., 6/6, partial. The fundi showed Grade-1 arteriolar sclerosis in each eye. The caliber of the arterioles was not abnormal. There were no focal constrictions. There were no hemorrhages or exudates. The macula of each eye was very slightly edematous and showed very fine pigment stippling. The foveal depression could not be seen in either eye. In the right eye there were numerous fluffy vitreous floaters.

The patient was given a complete medical examination. Nothing of note was found save for an early arteriolar sclerosis and a blood pressure of 150/84 mm. Hg. The patient was placed on a vasodilator (tablets, roniacol, 50 mg., three times daily before meals). After two months' treatment patient stated she felt better and that vision was definitely improved. She now could read with ease.

Examination showed little change in the fundi and the visual acuity was: R.E., 6/9; L.E., 6/7.

Diagnosis. Senile macular degeneration.

CASE 13

M. F. E., a woman, was seen first in June, 1949, at the age of 72 years.

The patient complained that she had had blurred vision for the previous two or three months. She had suffered from high blood pressure for many years. The patient was a rather nervous, birdlike individual. She had no well-marked anxieties but was chronically worried about finances even though quite well off.

She had 6/9 vision, R.E., and 6/60 vision, L.E. Fundus examination showed Grade-1 arteriolar constriction and Grade-1 arteriolar sclerosis. There were very fine pigment changes in the right macular region. The left macula showed a large cystlike rarefaction. There were no hemorrhages or exudates.

A general medical examination was essentially negative except for a blood pressure of 180/95 mm. Hg.

Since the first visit, the patient has remained essentially unchanged though the right fovea from time to time has shown very slight edema. There has been no change in the visual acuity. The patient has been treated from time to time with nicotinic acid and priscoline and she has been on a continued high dosage of vitamin-B complex.

Diagnosis. (1) Hypertension with early arteriolar sclerosis; (2) senile macular degeneration.

CASE 14

G. E. E. N., a woman, was first seen in April, 1950, at the age of 73 years.

The patient stated that for a year previous to examination she had noticed failing vision. At examination she had 6/240 vision in each eye which could not be improved by any correction.

Examination showed a mild degree of generalized arteriolar narrowing (grade 1) and a moderate degree of arteriolar sclerosis (grade 2). The venules were mildly compressed where crossed by the arterioles but not engorged or tortuous. There were no hemorrhages or exudates. There was quite marked edema of each macula which also showed mottled pigmented and rarefied areas.

The patient had had mild hypertension for many years. General medical examination at the time of her eye examination showed a blood pressure of 170/85 mm. Hg. There was no other evidence of any other systemic disease. The patient was a highly energetic, active individual, but had no particular anxieties.

The patient was placed on priscoline (25 mg., three times daily) and rutin. This therapy was continued for over a year, during which time there was no improvement in her vision, though the edema of the macula on each side disappeared leaving a scarified area.

Diagnosis. (1) Hypertension, arteriolar sclerosis; (2) senile macular degeneration.

CASE 15

R. H., a woman, was seen first in February, 1950, at the age of 66 years.

The patient had been highly myopic all her life. Six months before her first examination she had a mild coronary occlusion. The patient was a somewhat high strung, nervous individual, but had no apparent anxieties. For three months the patient had been unable to see enough to read.

Examination showed that the patient required a —8.5D. sph. to correct each eye. With this correction she read 6/15, R.E.; 6/9, L.E.

The fundus examination showed a rather large myopic crescent in each eye. Both maculas showed a moderate degree of simple edema. The arterioles showed Grade-1 sclerosis and Grade-1 generalized constriction. There were no hemorrhages or exudates.

Medical examination was negative except for a mild hypertension of 160/90 mm. Hg. and a nodule that was found in the left breast. This nodule was thought to be suggestive of cancer and a radical mastectomy was carried out.

The patient was placed on priscoline and rutin immediately after the first eye examination. This has been continued until the present.

At the last examination there was fine pigment mottling in each macular region but there was no edema. There was an early nuclear cataract in each eye which was not apparent at the first examination. With correction vision was: R.E., 6/20; L.E., 6/30.

Diagnosis. Mild hypertension and arteriolar sclerosis with senile macular degeneration.

CASE 16

W. J. H., a man, was first seen in July, 1947, at the age of 70 years.

The patient was referred because of senile cataracts. The vision was 6/60 in each eye. He was a somewhat nervous high-strung individual with no emotional disturbances determinable.

Medical examination was negative except the patient had moderately high blood pressure, 180/95 mm. Hg.

In October, 1949, on the right eye, a cataract extraction was performed with a round pupil and two peripheral iridectomies. The patient made an excellent and uneventful recovery. On November 24th, the patient was supplied with glasses, at which time the vision was 6/12 with the right eye. The fundus appeared normal.

The patient returned in January, 1950, stating that the vision in the right eye appeared blurred, which varied from time to time. Examination showed that he had 6/18 vision in this eye.

In the fundus the arterioles showed Grade-1 general constriction and Grade-1 sclerosis. There were no hemorrhages or exudates, but the macula was edematous. Further, a prolapse of the vitreous had occurred into the anterior chamber and it had become adherent to the corneoscleral margin on the nasal side. This latter resisted all attempts, including an air injection, to replace.

Since this examination the edema of the right macula has varied from time to time, but in the last six months it has disappeared leaving a very fine pigment mottling. The patient was supplied with nicotinic acid to use during the active stage of his disease. At present the vision of the right eye, with correction, is 6/18.

Diagnosis. (1) Aphakia with prolapse of vitreous into the anterior chamber; (2) moderate hypertension with early arteriosclerosis; (3) senile macular degeneration.

CASE 17

C. P. M., a woman, was first seen in January, 1950, at the age of 64 years.

The patient stated that the vision in the left eye had been poor for about 18 months. In the previous two or three months, the vision in the right eye also had been getting worse slowly.

The patient was rather an excitable, but not a neurotic type of individual. She had moderately high blood pressure, 170/95 mm. Hg. She had suffered from the cold for years, and had mild intermittent claudication when walking. The patient was terrified that she was going blind.

Examination showed vision to be: R.E., 6/60; L.E., 6/240. The fundi showed Grade-1 arteriolar sclerosis and Grade-1 generalized arteriolar constriction. The macula of the left eye was atrophic showing mottled pale and pigmented areas. The macula of the right eye was quite markedly edematous with mild pigment mottling. There were no hemorrhages or exudates.

The patient was put on nicotinic acid and rutin. In three months the vision in the right eye had improved to 6/12 but that in the left remained at 6/240. The fundi, however, appeared about the same. The patient stated that she was feeling much better and was not worrying now about going blind.

With mild exacerbations from time to time the patient has continued to show improvement so that now the vision is: R.E., 6/7; L.E., 6/120. The left macular region still shows mottled pigmented and atrophic areas. The right macular region shows very fine pigment stippling but no edema. The vision is: R.E., 6/7; L.E., 6/120. The patient is continuing with vasodilators.

Diagnosis. (1) Moderate hypertension and mild arteriolar sclerosis; (2) senile macular degeneration.

CASE 18

G. C., a man, was seen first in August, 1944, at the age of 26 years.

The patient was a notable fighter pilot during World War II. He had been decorated for bravery with the D.S.O. and D.F.C. In 1944, while on his second tour of duty as a fighter pilot he suddenly noticed one day that he could not see with the left eye.

Examination showed that he had a large hemorrhage in the macular region. This appeared to be subretinal. No spasm or sclerosis of the retinal arterioles was apparent. Gradually over the next two months the hemorrhage subsided and was replaced by a large pale sclerosed area with mottled pigmentation.

The patient was left with an absolute central scotoma. Vision was: R.E. 6/6; L.E., 6/240 (by eccentric fixation).

The general medical examination was negative and the blood pressure was 120/75 mm. Hg.

The patient was exceedingly intelligent and of a rather sensitive nature. He had a very strong sense of duty. The patient stated that he always had liked flying but that it produced nervous tension. He stated that his operational duty caused great mental stress, though he was able to fly in spite of this. It is interesting to note that he flew successfully on operations for some time before reporting his visual defect.

Diagnosis. Central angiospastic retinopathy. (Kuhnt-Junius type).

CASE 19

H. G., a woman, was first seen in March, 1948, at the age of 55 years.

The patient is a high-strung, nervous, and sensitive woman. During her menopause which took place seven years previous to the above date she had a nervous breakdown associated with a marked phobia for food. She made a good recovery from this.

Seven months previous to the present visit her mother-in-law came to live with her. The patient felt it her duty to look after her, though the two were very antipathetic. About two months after this she consulted an oculist to have her eyes checked for glasses as she had moderate myopia.

Examination showed that, with correction, she had 6/60 vision in the right eye, and 6/6 in the left. The fundi showed no arteriolar sclerosis nor arteriolar spasm. There was a large area of edema in the right macula with some pigment mottling. The left macula was normal.

The patient was completely checked with a view to discovering any foci of infection or allergies. None were found. The blood pressure was 135/75 mm. Hg. She was placed on nicotinic acid and rutin. Though the edema in the right macular region improved it was replaced gradually by scar tissue. The vision in the right eye never improved above 6/240.

The patient returned in April, 1949, with some failure of vision in the left eye. She had been under great stress owing to the illness of her mother-in-law when she had to do all the nursing.

Examination showed that the right macular region was quiet, though greatly scarred. The left macula appeared slightly edematous. The corrected vision was: R.E., 6/240; L. E., 6/7, partial. The patient was given no treatment but kept under observation.

In December, 1949, her household affairs became very difficult again and the vision in the right eye became poor again. On examination, vision was: R.E., 6/240; L.E., 6/7, partial. The right fundus was unchanged; the left macular region showed a moderate degree of edema with a pale ring about the fovea suggesting the margin of a cyst. The patient was placed on rutin and nicotinic acid.

By March, 1950, the vision was: R.E., 6/240; L.E., 6/6. The right fundus was unchanged. In the left eye there was mild macular edema, with very fine pigment stippling in the foveal region. There was no evidence of any cyst in the fovea.

Since that time, the patient has had minor exacerbations in the left eye on two occasions, each precipitated apparently by family trouble. On each occasion the patient was placed on rutin and nicotinic acid for approximately six weeks. The vision in the left eye has returned always to 6/6. In the right eye it is 6/480.

Diagnosis. Central angiospastic retinopathy.

CASE 20

J. J. M., a man, was first seen in February, 1944, aged 48 years.

The patient first consulted a confrere complaining of poor vision in the left eye for about a month.

Examination showed that he had vision of: R.E., 6/6; L.E., 6/9. The right fundus was essentially negative. The left fundus showed a large buff-colored area in the macula. In the upper margin of this area and just below the upper left temporal arteriole were two small white areas composed possibly of white exudate. A month later two small hemorrhages appeared in this upper region.

The patient was examined competely for foci of infection and any other abnormalities. None were found, except for an increased density of the left maxillary sinus. This was washed out and a nonhemolytic streptococcus was found. A vaccine was prepared to which he gave a positive skin test. The patient was then desensitized with an autogenous vaccine. The cardiovascular system was normal, the blood pressure was 130/80 mm. Hg.

Owing to the retirement of my confrere, the patient now came under my care. The left macula region gradually quietened. The hemorrhages disappeared. The pale area changed into atrophied retina with mottled pigment around the margin. The right fundus remained normal. Desensitizing injections were carried over a period of the next year and a half.

In April, 1948, the patient complained that he had a blurred area near the center of the vision in in the right eye. Examination showed that he had 6/6 vision, right eye, and 6/60 vision, left. The left fundus showed a large, pale, atrophic area in the macula which was unchanged. There was a small pale area of edematous retina just up and to the nasal side of the right fovea occurring at the end of a small branch of the celioretinal arteriole.

The patient again was completely examined and no evidence of any active disease of any sort was found. A complete allergic work-up was negative. The patient's histamine sensitivity was tested and found to be normal.

By June, 1948, the original pale area in the right fundus disappeared and now the fovea itself appeared slightly edematous, and there was a very faint almost cystlike appearance in the fovea itself. However, the vision in the right eye remained at 6/6, partial, though in subdued light the patient could see a shadow in the center of the right vision. The patient was placed on nicotinic acid and rutin.

By January, 1951, the central relative scotoma had disappeared. Vision was: R.E., 6/6; L.E., 6/60. The right fovea showed very fine pigment mottling but no edema. The vessels appeared quite normal. The left showed the original large area of macular degeneration.

During the period from 1948 to 1951 and before final recovery, the patient had periods of mild exacerbation but with improvement each time of the vision in the right eye. During each exacerbation, the patient was placed on nicotinic acid and rutin. Each exacerbation appeared to be associated with some emotional disturbance related to either a death or illness in the family, or some financial worry.

During the last year the condition has been perfectly quiet and there has been normal vision in the right eye.

Diagnosis. Central angiospastic retinopathy.

CASE 21

E. S. M., a woman, was first seen in August, 1946, aged 51 years.

The patient always has been a fragile, highly nervous individual. She has been troubled with bronchitis and asthma for years, and has frequent attacks of dermatitis, apparently of a nervous or allergic type.

When first seen she had 6/6, partial, vision in each eye and the fundi were quite normal. She was seen at intervals following this time for routine examination and refraction. During the autumn of 1949 the patient was under great strain owing to the serious illness of her husband. He developed and was operated upon for carcinoma of the larynx. During this time she had an exacerbation of her bronchial trouble and of her dermatitis. The blood pressure was 120/70 mm. Hg.

She came to the office in November, 1949, one month after the husband's operation, stating the vision in the right eye had been very blurred for two weeks. Examination showed that her vision was: R.E., 6/120; L.E., 6/6. The right fundus showed the macula markedly edematous but the vessels were quite normal. There were no hemorrhages or exudates. The left fundus was quite normal. The patient was placed on rutin and nicotinic acid.

By January, 1950, the vision had returned to 6/6 in each eye and the fundi were quite normal. On repeated examination since that time, there has been no evidence of any recurrence.

Diagnosis. Central angiospastic retinopathy.

CASE 22

E. C. N., a man, was seen first in May, 1943, at the age of 45 years.

While on wartime duty, the patient suddenly noticed that he had a blurred spot in the center of the vision of the left eye. Examination showed that he had vision of: R.E., 6/6; L.E., 6/18. This blurred spot was due to a relative central scotoma in the left eye.

Fundus examination of the right eye was quite normal but in the left eye there was a relatively well-circumscribed area of edema in the macular region. Running into the upper border of this area was a small vessel arising from the upper left temporal arteriole. This vessel was markedly spastic. The other arterioles of both fundi were quite normal. There were no hemorrhages or exudates.

The patient while on duty had been long separated from his family. He had a rather large family which by nature always seemed to be getting into some sort of trouble. Though not of a neurotic nature the patient was thus constantly in anxiety. He had a position of considerable difficulty and responsibility in the service. The general medical status was checked and was found quite normal. The blood pressure was 130/75 mm. Hg.

After investigation, the patient was returned to his home for convalescence and rest. No particular treatment was carried out. The patient completely recovered spontaneously in about two months.

Diagnosis. Central angiospastic retinopathy.

CASE 23

T. N. O., a man, was first seen in March, 1949, aged 30 years.

The patient was a salesman with a territory in Eastern Canada. His home office was in Newfoundland where his wife and only child lived. He stated that every time he left home either his wife or child would become ill so that he took each trip with great anxiety.

On the present occasion he had left home and had just arrived in Montreal when he received a telegram stating that his daughter was very ill and asking him to return home immediately. However, he could not get home because of bad weather which had closed down all airports in Eastern Canada. The next morning he awoke and found the vision in the left eye exceedingly blurred.

Examination showed he had 6/6 vision, right eye, and 6/60 vision, left. The fundi showed normal vessels. The arterioles were not constricted, nor was there any arteriolar sclerosis. The right macular region was quite normal but the left one was markedly edematous and there was a small flame-shaped hemorrhage arising from a small branch off the upper left temporal arteriole just above the fovea.

The patient was completely checked over but no systemic disease was found. The blood pressure was 125/75 mm. Hg. The patient was put on nicotinic acid 50 mg., three times daily) and rutin. Within a month the condition subsided. The vision was: R.E., 6/6; L.E., 6/6. Just a small amount of faint pigment stippling remained in the left macular region.

Diagnosis. Central angiospastic retinopathy.

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THE USE OF HYALURONIDASE IN OPHTHALMOLOGY*

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The purpose of this paper is to evaluate the use of hyaluronidase in the nonsurgical treatment of pterygiums and to report other uses of the drug in ophthalmology.

Pterygiums of the eye are a very common disease in Panama. The reasons that they are so prevalent in this tropical area are the improper nutrition in the poorer classes of people and such local irritating factors to the eyes as the tropical sun, dusty dry season, and occupations about the water fronts. Since pterygiums are a constant problem in the tropics, it was felt that any new development of a nonsurgical treatment would be of value in the management of this disease.

HISTORY AND PROPERTIES OF HYALURONIDASE

Hyaluronic acid, one of the main substances of the intercellular substance was first isolated by Meyer and Palmer.[1] In 1929, Duran-Reynals[2] proposed a "spreading factor" in the spread of tissue infection. Duthie and Chain[3] demonstrated that the enzyme, hyaluronidase, liquefied the tissue cement substance, hyaluronic acid, which explained the mechanism of the "spreading factor" by Duran-Reynals. This occurs by the depolymerization of the hyaluronate through the hydrolysis of the linkages with the decrease in the viscosity of the polysaccharide, hyaluronic acid, allowing more rapid spread of fluids through connective tissue.

Hyaluronidase is a proteinlike substance, easily destroyed by pepsin and trypsin, soluble in water and dilute acids, insoluble in alcohol, and inactivated by heat and ultraviolet radiation. The enzyme functions at a more rapid rate under the influence of pressure. Also diffusion of solutions is dependent upon two factors; the amount of solution present and the dosage of the enzyme used.[4]

The action of hyaluronidase is reversible with complete restoration of the intercement substance in 24 hours.[5] The enzyme presents no toxicity and in our experience no allergic manifestations have appeared.

Hyaluronidase available to us was in vials containing 150 turbidity reducing units under the trade names of Hydase (Wyeth, Inc.),

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Hyronase (Schering Corp.).† One turbidity-reducing unit is defined as the amount of enzyme per cc. which, acting on 0.2 mg. hyaluronic acid at incubator temperature for 30 minutes, reduces the turbidity in the test to that given by 0.1 mg. normally aggregated hyaluronic acid.

Treatment of pterygiums

Lebensohn[4] noted that small pterygiums were probably benefited by the subconjunctival injection of hyaluronidase. In order to determine the value of hyaluronidase in the treatment of pterygiums, 40 patients with pterygiums in various stages of maturity underwent this form of therapy at Gorgas Hospital, Panama Canal Zone. We used two commercial products: Hydase (Wyeth, Inc.) in vials of 150 turbidity-reducing units, and Hyronase (Schering Corp). in vials of 150 and five turbidity-reducing units.

Due to the pain associated with the subconjunctival injection of distilled water following topical anesthesia, it was found advisable to use one-percent novocain mixed with hyaluronidase; 0.3 to 0.4 cc. of hyaluronidase-novocain solution was injected at a border of the pterygium with a 25-gauge needle pointing at the limbus, with the subsequent ballooning up of the pterygium away from the sclera.

Types treated

Five types of pterygium in different stages of maturity were encountered in this series of study:

1. Small, fleshy, vascular growth not extending onto the cornea (15 cases).

2. Fleshy and vascular growths extending onto the cornea for one mm. (13 cases).

3. Dense, fibrous growth extending onto the cornea with much scarring of the corneal area involved (five cases).

4. Pterygium recurring after surgery (five cases).

5. So-called malignant pterygium with rapid growth of a fleshy, vascular tissue extending rapidly over the cornea (two cases).

Results

It was found that uniform changes resulted with the use of 50 hyaluronidase turbidity-reducing units with each subconjunctival injection and that the use of any larger dose of hyaluronidase did not improve the results. If the pterygium responded to the treatment, usually only three injections were necessary with a one-week interval between each injection.

None of the patients complained of any pain or discomfort from the injection of the novocain-hyaluronidase solution into the bulbar conjunctiva. No allergic manifestations were noted in this series of cases.

Several of the pterygium cases treated had other complications present such as healed keratitis, inactive iritis, senile cataracts, and healed chorioretinitis. None of these conditions were altered or aggravated by the use of the subconjunctival hyaluronidase.

Twenty-four hours after the injection of hyaluronidase the pterygium under treatment became pale, edematous, and less vascular, but with increased vascularity of the conjunctiva surrounding it. The conjunctival injection subsided in a few days.

With the type-1 pterygium, with no encroachment of the cornea, the pterygium assumes the appearance of normal conjunctiva after two or three treatments over a two- or three-week period.

With the type-2 pterygium, the apex of the pterygium becomes paler and shrinks toward the limbus. The amount of regression is not significant if the apex of pterygium encroaches more than one mm. on the cornea.

In type-3 pterygium, where the apex of the pterygium is less vascular and fibrotic, there is very little tendency for the growth to regress in size. However, it was noted that

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† Wyeth, Inc., and Schering Corporation generously supplied the hyaluronidase used in this clinical investigation.

the head of the pterygium was usually less vascular following treatment.

In those cases of type-4 pterygium, where the growth recurred following surgery, the use of hyaluronidase caused the recurrent pterygium to become edematous and vascular, but did not cause regression of the pterygium.

In the malignant pterygium, type-5, the hyalurondiase had no effect and it was found necessary to resect the pterygium and treat it with soft X rays.

Pathologic study

With those patients who had bilateral pterygiums, one pterygium was given a series of treatments with hyaluronidase, while the other pterygium was not treated. Both pterygiums were then resected for pathologic study. In comparison, the sections of the pterygium treated with hyaluronidase revealed a marked loss in the amount of elastosis present, and also the metaplasia of the epithelium was much less.

Conclusion

Thus in our experience the use of hyaluronidase is of value in the treatment of early pterygiums of the eye, the types 1 and 2 of this series. It caused complete disappearance of the pterygium and the return to the normal appearance of conjunctiva if the pterygium was fleshy, vascular, and if the apex of the pterygium had not encroached on the cornea more than one mm.

If the pterygium was old, fibrous, and avascular, the hyaluronidase did not cause regression of the pterygium and surgical intervention was necessary.

Other uses of hyaluronidase

During our pterygium studies, several different types of ocular disease were treated with hyaluronidase in order to establish other uses of the drug.

1. Four cases of traumatic subconjunctival hemorrhage were treated with the subconjunctival injection of a hyalurondiase-novocain solution. These hemorrhages were early and extensive. In four days, after two injections of hyaluronidase (50 turbidity-reducing units) the hemorrhage had completely reabsorbed. It was felt that the reabsorption period of the hemorrhage was definitely reduced by the use of the hyaluronidase.

2. Two cases of early, mild episcleritis were treated with subconjunctival injection of hyaluronidase (50 units) each. After two injections over a five-day period, there was no clinical evidence of the episcleritis. In one case of severe nodular episcleritis the drug had no effect.

3. A 50-year-old man, with a progressive, marginal degenerative process of the cornea of 15 years' duration with marked bilateral limbal degeneration and ciliary injection, was given eight injections of hyaluronidase (50 units) in each eye over a two-month period. After each treatment it was noted that the calcified area was less and that the ciliary injection had regressed.

Upon completion of the treatment, the degenerative area was markedly reduced in one eye and completely gone in the other. The patient has been asymptomatic over a six-month period since cessation of the treatments. It was of interest to note that this patient was allergic to the sulfonamides, penicillin, atropine, and scopolamine, and yet did not manifest any allergic signs or symptoms while treated with hyalurondiase.

4. Fifteen patients of the Palo Seco Leper Colony, Panama Canal Zone, with old iritis of long standing were treated with hyaluronidase. These cases of old leprous iritis presented dense posterior synechias, no flare, nor any signs of activity.

All the patients were placed on local instillation of atropine (one percent). Half of the patients were given four injections of hyaluronidase (50 units) mixed with 0.2 cc. of adrenalin at the limbal margin over a two month period. In the other half of the patients the adrenalin was not used in conjunction with the hyaluronidase.

This endeavor to release the posterior synechias was futile. The patients did not exhibit any side reactions from the use of the hyaluronidase.

5. Atkinson[6] reported that the use of hyaluronidase, procaine, and epinephrine in the retrobulbar injection for surgical anesthesia caused the surgical procedure to be more difficult. It was thought that, because of the hypotony associated with this type of anesthesia, it might be of definite value in the surgical removal of a dislocated lens in the presence of secondary glaucoma.

In the one case of dislocated lens with increased intraocular pressure in which hyaluronidase was used with the procaine-epinephrine retrobular anesthesia, the tension was markedly reduced after the retrobulbar injection, and it was felt that the decreased tension was of definite aid in removing the lens without the loss of vitreous.

6. The use of hyaluronidase in the vitreous or the anterior chamber is not advisable because of severe inflammatory reaction as was noted in rabbit studies in which hyaluronidase, mixed with spinal fluid, was injected into the vitreous and anterior chamber of the rabbit's eye. This is in agreement with the findings of Lebensohn.[4]

7. In the treatment of keratitis and iritis with subconjunctival injections of cortisone, it was found that if the 0.6 cc. of the cortisone was mixed with hyaluronidase (100 units) and injected subconjunctivally the cortisone was spread over a greater subconjunctival area, was more homogenized in nature, and that the absorption time from the subconjunctival area was lessened. How beneficial this is to the actual disease process will have to await more complete statistical studies.

Summary

Hyaluronidase appears to be of value when a spreading factor is desired either as a primary action or in the dispersion of drugs. A reaction to this spreading factor appears to be increased circulation to the area involved.

Conclusions

1. Hyaluronidase injected into early pterygiums caused resolution of the growth in our series if there was not more than one mm. progression of the apex onto the cornea.

2. Hyaluronidase hastened reabsorption of subconjunctival hemorrhages.

3. Hyaluronidase had a beneficial effect on one case of degenerative keratitis with dissolution of some of the degenerative products of the cornea.

4. Hyaluronidase was not found to be beneficial in freeing posterior synechias of leprous iritis of long standing.

5. In retrobulbar anesthesia, hyaluronidase may be a valuable adjunct when hypotony is desirable as in the removal of a dislocated lens when increased ocular tension is present.

6. It was found inadvisable to use hyaluronidase in the anterior chamber or vitreous.

7. Hyaluronidase may be of value in hastening the absorption of cortisone injected subconjunctivally.

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CENTRAL ANGIOSPASTIC RETINOPATHY

A REVIEW OF THE LITERATURE AND REPORT OF ONE CASE

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In 1866 von Graefe[1] described a condition of the macular region in which there apparently occurred a circulatory disturbance. He gave the name of central recurrent retinitis to this disturbance. Since then, a number of authors have described similar pictures and given different names to what appears to be the same disorder.

In 1898, Asayama (cited by Gifford and Marquardt[2]) described the lesion, rather frequent in Japan, to which he gave the name retinitis centralis. In 1916, Fuchs[3] described a condition to which he gave the same name that von Graefe had originally used. In 1921, Batten[4] described a temporary disease of the macula of favorable prognosis.

Guist[5] and Gissy,[6] in 1925, independently described what they called cases of preretinal edema. Weintraub (cited by Walsh and Sloan[7]) reported a case to which he gave the name of just plain macular edema. In 1936, Walsh and Sloan,[7] in the United States, wrote about a condition they called idiopathic flat detachment of the macula.

Horniker[8] described cases of short obscurations of vision associated frequently with a history of asthma, claudication, and angioneurotic edema. Vasodilators brought prompt relief in his patients. He proposed the term central angiospastic retinitis for the condition.

Bailliart,[9] believing there was an inflammatory change in the capillaries near the macular region, called the condition retinal capillaritis. Gifford and Marquardt,[2] in 1938, described new cases and proposed the name central angiospastic retinopathy.

Cattaneo[10] called it a retinal capillarosis; Candian,[11] angioneurotic macular degeneration; Junius (cited by Duggan,[12]) preferred the term juvenile exudative macular retinitis. In 1938, Ricker (cited by Duggan[12]) termed this lesion choroidosis centralis serosa.

Asiatic authors have preferred to call it chorioretinitis centralis serosa. Most authorities agree that the term central chorioretinitis and retinitis centralis are not appropriate for this condition because the course and sequalae are unlike those of the central retinitis and chorioretinitis commonly observed.

ETIOLOGY

Many and varied theories have been offered to explain the etiology of this condition. Both von Graefe[1] and Fuchs[3] attributed the disorder to syphilis, the scrap pile of practically every disease whose cause is not clear.

Batten,[4] on the other hand, believed the cause of this condition to be toxic. Kraupa[13] attributed the changes in the macula to ischemia, the result of disturbances of the circulation of the blood. Guist[5] and Gissy[6] independently gave tuberculosis as the etiologic factor in these cases.

Walsh and Sloan[7] concluded from their studies that the factor behind these cases was a toxic one. These authors' cases were carefully studied: some foci were found and treated but no definite cause was found.

Horniker[8] collected 43 cases in which he showed definite evidences of instability of the vasomotor system. He confirmed this by the so-called method of entoscopy. He believed that an ischemia was produced by a functional narrowing of the finer retinal arterioles or capillaries. Psychic disturbances, exposure to cold, and in a few cases exposure to excessive light, were, in his opinion, precipitating factors. He believed that syphilis and tuberculosis, when they existed,

acted only as contributing factors in persons with a vasoneurotic diathesis.

Bailliart[9] observed a phenomenon similar to the one described by Horniker, in old people with hypertension.

Gifford and Marquardt,[2] in 1938, made an extensive review of the whole subject and established the fact that a circulatory instability is the etiologic factor in many cases. They stated that the symptoms and changes noted are best explained as the result of spastic contraction of the smaller retinal arterioles or capillaries supplying the macular region. As they stated, a temporary closure of the central retinal arteries is a well-known condition. But the disease under discussion is the result of constriction of a number of smaller vessels supplying the macular region, not a closure of the larger arteries. These authors did not believe there was an inflammatory basis to this disturbance.

Duke-Elder[14] has the impression that the majority of these cases have a toxic basis, probably of an allergic nature. It may be of significance that the majority of the cases which he has seen have had a highly positive skin reaction to tuberculo-protein, a reaction which as he says, need not necessarily be specific.

Batten[4] described a condition in young males the cause of which he believed to be septic. Oguchi[16] believed paranasal sinusitis the cause of this disorder and thought it to be inflammatory in origin.

All of Gifford and Marquardt's[2] cases gave a negative Wassermann reaction and did not show any evidence of tuberculosis. Verhoeff and Grossman,[16] in discussing serous retinitis, expressed the thought that its cause may be a serous exudation from the choroid. They also stated that their observations in their cases did not exclude the possibility of a localized vascular lesion.

Duggan[12] attributed the etiology of his cases to different factors. In one of his patients, for instance, he believed the cause of the disorder to a hypersensitivity to cold which was, therefore, attributable directly to histamine. Another case he believed may have been due to iodides injected intravenously. Some of his patients were heavy smokers. In one other case the lesion probably followed a cold. Another patient was a "high-strung" woman in whom excessive circulating epinephrine may have brought on the condition. Two other patients were arteriosclerotic.

Duggan also believed that meteorologic factors might be responsible for this disorder. So did Petersen,[18] who showed the simple relationship existing between the precipitation of acute vascular episodes in the eye and the meteorologic environment in which a patient lives. Meteorologic alterations produce pressor episodes which interfere with the supply of blood to the tissues.

Moon[17] has demonstrated that increased capillary permeability leads to capillary anoxia with an ensuing tissue anoxia which results in a depression in function of the anoxic tissues. Capillary permeability may be increased beyond physiologic limits by insufficient oxygen in the circulating blood, histamine, venoms, certain drugs, especially arsenic and iodides, by lack of cevitamic acid, and by excessive arteriolar constriction. The latter phenomenon can be produced by epinephrine, nicotine, histamine, and other substances.

Localized tissue anoxia produces lesions which have been attributed to allergy, focal infection, or tuberculosis. These lesions are due to changes in the blood vessels which are of physiologic nature but of pathologic degree.

Incidence

According to Duke-Elder,[14] central angiospastic retinopathy occurs in young or middle-aged people, especially males. Gifford and Marquardt[2] stated that the average age is 40 years. These authors also remarked that it is twice as frequent in males as in females.

It seems probable, according to Walsh and Sloan,[7] that many of the patients with this disease may never seek advice because of

the slight loss of vision and the marked tendency to spontaneous recovery. Some cases may be erroneously diagnosed retrobulbar neuritis.

Symptoms

Central angiospastic retinopathy is characterized by recurrent transient attacks of loss of vision with complete or almost complete restoration of vision. The relapses are of lessened severity according to the findings of Walsh and Sloan.[7] A central blurring of vision is the usual presenting symptom. A visual acuity of 20/20 does not rule out a lesion of this nature.

The condition is further characterized by a transient hyperopia and a positive central scotoma. The hyperopia is usually demonstrable only if the visual acuity is nearly normal. Abe[19] explained the hyperopia as being due to retinal edema.

Kitahara[20] reported a series of cases in which quiescence occurred in two to three months, but in which recurrences were common. One of his patients had 14 recurrences in a period of three years.

Micropsia may be another symptom complained of, according to Duggan.[12] This, however, is a symptom only when there is little or no gross reduction of visual acuity or when the lesion is not exactly central in location. Metamorphosia may also be complained of occasionally.

Only one eye is involved at a time according to Walsh and Sloan.[7]

The symptoms originate as the result of a spasm of the capillaries of the macular area affecting the especially vulnerable area of the central retina.

Insofar as symptoms referable to other parts of the body are concerned, Gifford and Marquardt[2] have found that patients having central angiospastic retinopathy have subjective symptoms of coldness and paresthesias of the extremities. Blanching of the hands and feet when these are exposed to cold or washed in cold water suggests a peripheral angiospasm. The extremities of these patients flush in the dependent position and become pale on elevation also.

Ophthalmoscopic findings

Ophthalmoscopic examination of this disease entity reveals an edema limited to the macular area, according to Duke-Elder.[14] The edema is frequently slight and can best be visualized by observing the affected area with the periphery of the reflected light of the ordinary May ophthalmoscope. The attack is followed by minimal atrophic changes.

The edema frequently shows small exudative spots which vary in color from white to yellow. Bailliart[9] believed these spots to be due to isolated ischemia following closure of the capillaries with a deposit of lipoid material to replace degenerated cells.

Pigmentary deposits may be left behind after the edema disappears. In this connection Duggan[12] has stated that this pigmentation is characteristic of choroidal lesions. Many cases show nothing except a slightly darker hue in the macula and no foveal reflex.

Guist[5] noted a peculiar ring-shaped reflex which he believed was due to fluid between the inner surface of the retina and the vitreous.

It should be emphasized that the ophthalmoscopic findings are minimal in the early stages of the condition. They may easily be overlooked by ordinary ophthalmoscopic examination and a diagnosis of retrobulbar neuritis may be made. Careful examination with the Friedenwald ophthalmoscope or by means of the red-free light will reveal signs of retinal edema localizing the disorder in the retina.

According to Cattaneo[10] the lesion may be macular, paramacular, or disseminated. This, as Masuda (cited by Duke-Elder[14]) stated, was due to subretinal exudate. Oguchi[15] believed the exudate originated from the choriocapillaries and that this lifted the retina from the choroid and thereafter passed into the retina. Walsh and Sloan[7] likewise believed the edema to be subretinal in location, a fact which explains why these two authors pre-

ferred the term idiopathic flat detachment of the macula for this disturbance.

Walsh and Sloan[7] remarked that the transitory hyperopia and elevation of the macular region up to three or four diopters are the important objective findings in this disease. The temporary hyperopia in these cases is obviously due to a shortening of the optic axis, these authorities stated. This can be roughly estimated by focusing on the macula of each eye with the ordinary ophthalmoscope.

According to Walsh and Sloan, the disease under consideration tends to be self-limited and the macular protusion commences to flatten within a few weeks. However, the yellowish spots increase in number. The protrusion disappears then or is greatly reduced.

Guist[5] and Gissy,[6] independently have reported abnormal foveal reflexes. From his observations, Guist[5] concluded that there was a transparent biconvex layer of fluid in front of the retina.

Walsh and Sloan[7] have described what they see on ophthalmoscopic examination as follows: "The retinal vessels come forward sharply at the margin of the affected area and retain their superficial position over the entire elevated area."

In two of their cases they noted a reduplication beam with the Friedenwald ophthalmoscope, a fact which proved to them the presence of two reflecting surfaces separated by an optically clear space. It was their opinion that the anterior of the two surfaces was the retina while the posterior one was the pigment epithelium. These writers also observed that the hyperopia decreased as the macular swelling diminished and that the percipient elements in the macular region were displaced forward by the edema.

Diagnosis

The diagnosis of central angiospastic retinopathy is made on the basis of the physical examination of the eye with the ordinary ophthalmoscope, the Friedenwald instrument and/or the binocular ophthalmoscope, on the serologic examination, and on a careful history with particular reference to subjective symptoms of coldness and paresthesias of the extremities.

A blanching of the hands and feet upon immersion in cold water suggests peripheral angiospasm. The nutrition of the skin and muscles and the color of the skin should be noted.

Gifford and Marquardt[2] recommend that the temperature of the skin be taken after the patient has been in a draft-free room for one hour. The temperature should not vary more than four to six degrees from that of the abdomen. Lower temperature readings than this mean a deficiency of the arterial blood.

A diagnostic point of importance is a field defect which consists of a central scotoma both for white and colors. Characteristically the scotoma is larger for blue than for red.

Duggan[12] diagnosed the condition on the basis of the history of central blurring of vision or of micropsia, by tangent screen scotometry findings at one meter, and by direct and indirect ophthalmoscopy with an ordinary light.

Walsh and Sloan[7] advocate the use of the binocular ophthalmoscope for accurate diagnosis of the disorder under consideration. The fact that this is not done often, these authors believe, accounts for the fact that the disease is not more widely recognized.

Differential diagnosis

Central angiospastic retinopathy has to be differentiated from retinitis centralis, angiospastic retinitis, and disciform degeneration of the macula. This lesion actually differs from acute exudative choroiditis quantitatively in that in the latter a complete atrophy of the nerve fibers passing over the lesion occurs, whereas, in central angiospastic retinopathy no such atrophy occurs.

The lesion has further to be differentiated from detachment of the retina in the macular area due to tumor, from central choroiditis in which the loss of vision is more marked, from retrobulbar neuritis, from actinic retinitis, where there is a history of exposure to heat and light, and from central recurrent syphi-

litic retinitis, which is severer and in which there is an alternating loss of vision in both eyes.

Prognosis

The prognosis of this disturbance is favorable. The edematous fluid in the macular area is absorbed, the retina returns to its original situation, and the visual acuity remains unchanged.

Treatment

Horniker's[8] treatment for this condition consisted of papaverine, atropine orally, barbiturates, and calcium to relax the peripheral vascular spasm. This treatment shortened and reduced the frequency and the severity of the recurrences.

Hery[21] recommended an insulin-free pancreatic extract.

Gifford and Marquardt,[2] like Horniker, directed their therapy toward the relief of the angiospasm. Accordingly they recommended the observation of hygienic measures and good habits by the patients suffering with this condition. Their regime prohibits the use of tobacco. Exposure to cold is likewise to be avoided. So is worry and excitement.

They advise the use of nitrites and typhoid vaccine intravenously, both of which agents are known vasodilators. In the experience of these authors papaverine hydrochloride in doses of 0.25 gr. intravenously is the most potent vasodilator for this disease.

My limited experience with this drug gives me reason to agree with this latter opinion. The drug is given three or four times a day, although they consider that once a day for short periods is enough.

Depropanex, a deproteinated pancreatic extract, may also benefit this disorder. This preparation, which is a vasodilator, is given every three or four days for a total of 12 injections. To take care of any possible emotional factors, barbiturates are recommended.

Walsh and Sloan[7] advise that all foci of infection be properly treated when present. Metabolic disturbances also, if present, should be corrected.

Report of a case

C. M. S., a 36-year-old white man, was seen by me on January 16, 1950, with the chief complaint of blurred vision in the right eye of three weeks' duration. On questioning, the patient stated that in 1945 he also noticed a gradual blurring of vision in the same right eye for which he was hospitalized for 15 days and discharged with recovery of his normal visual acuity. He stated that he had not been sick during the period of time immediately preceding the onset of his present illness. He also stated that he had never worn glasses. The past history was considered irrelevant. The patient was admitted to the hospital for diagnosis and treatment.

On admission the temperature, pulse, and respiration were well within normal limits.

Examination of the eyes showed vision without correction: O.D., 20/40+3; O.S., 20/20. There was slight conjunctival hyperemia and good anterior chambers, O.U. The pupils were round, regular, equal, reacted to light and accommodation directly and indirectly.

The muscle balance was normal. Tactile tension was normal, O.U. The media were clear. There was slight pallor of the macular area in the right eye, with absence of the foveal reflex. There were also few small yellow-white spots in the perifoveal area of the right eye (fig. 1).

Visual field studies. O.U.: peripheral visual fields and blindspots were within normal limits. O.D.: Small central scotoma demonstrated with the one-mm. white, red, and blue test objects (fig. 2).

Laboratory data. X-ray studies of the paranasal sinuses showed a moderate degree of cloudiness of the ethmoid cells bilaterally and of the lower one half of the right and of the major portion of the left antra due to mucous membrane thickening in

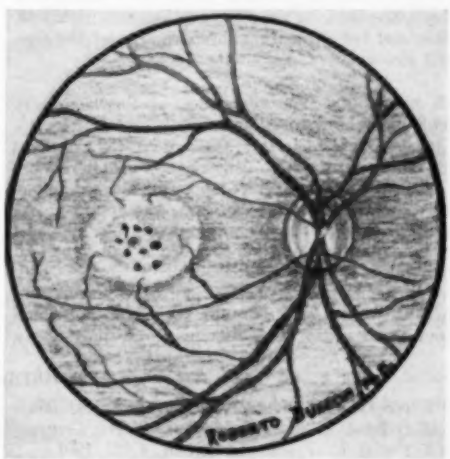

Fig. 1 (Buxeda). Appearance of the fundus of the patient's right eye upon admission to hospital. Notice the area of edema and the yellowish dots in the macular region.

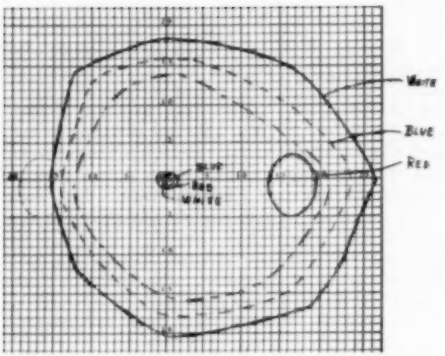

Fig. 2 (Buxeda). Visual field record on admission, showing the peripheral isopters and the outline of the central scotoma for white, blue, and red.

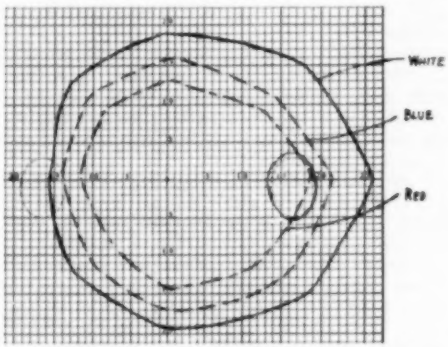

Fig. 3 (Buxeda). Visual field record just before discharge, showing the peripheral isopters for white, blue, and red. Notice the disappearance of the central scotoma.

all probability. The remainder of the laboratory findings were well within normal limits.

Course in the hospital. The patient was examined by the medical, genito-urinary, and dental services for possible foci of infection. None were found. However, a pedunculated mass was found in the vault of the palate. This was excised. Pathologic examination of the same revealed it to be the seat of chronic inflammation.

Immediately upon admission to the hospital the patient was started on 0.25 gr. of phenobarbital four times a day, multivitamins three times a day and Depropanex in doses of one cc. every four days. He was also given progressively increasing doses of typhoid vaccine intravenously every other day for five doses with a maximum dose of 130,000,000 killed typhoid organisms.

At the conclusion of the last vaccine treatment, 10 days later, the patient's visual acuity had improved to 20/30. The patient was then started on papaverine hydrochloride intravenously in doses of 0.25 gr. daily.

A week later the vision had improved to 20/20—1. At this time the central scotoma had also completely disappeared as shown by visual field studies (fig. 3). The patient was discharged 28 days after admission.

Comment

The accepted criteria for making a diagnosis of central angiospastic retinopathy are satisfied by the present case except for the absence of a report of peripheral vasospastic phenomena. These were not specifically looked for and it is felt that they were present in all probability. This fact, however, has not been made a requirement by most of the writers on this subject, although Gifford and Marquardt[2] do make a point of it.

The typical symptoms, the characteristic tangent screen findings of a central scotoma both for white and colors, which is characteristically larger for blue than for red, the ophthalmoscopic findings of macular edema, absent foveal reflex, and typical yellow-white dots in the macular region, plus the history of a previous similar episode and the complete remission of the present attack in a month's time, all justified the diagnosis which is the subject of this paper.

Summary

A review of the literature on central angiospastic retinopathy has been presented.

A case, the only one so far seen and diagnosed by me, is reported in detail. The criteria for arriving at this diagnosis are given.

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A METHOD OF LOWER LID RECONSTRUCTION*

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The variety of methods which have been proposed for reconstruction of the lower lid is evidence of the complexity of this problem. When lesions removed from the lower lid leave defects of less than one third of the lid, reconstruction is satisfactorily accomplished with V resections or with modified halving procedures, such as the lesser resection described by Reese.[1,2]

When defects of more than one half of the lid require reconstruction, the problem is more difficult. Two of the commonly used procedures at the present time are the greater resection described by Reese and the method of total lid halving described by Hughes.[2,3]

There are certain objections to both methods. The greater resection provides reconstruction of the lid composed of a sliding skin flap from the temporal region and conjunctiva salvaged from the inner surface of the lid to be excised. This does not permit block dissection of the lid when necessary and provides no method for reconstruction of tarsus for support when more than one half of the tarsus has been removed.

The method described by Hughes consists of halving the upper lid to supply conjunctiva and tarsus for the new lower lid and of sliding skin up from the cheek and remainder of the lower lid to supply a dermal surface for the new lower lid. In our hands this has frequently resulted in an unduly widened lid fissure and at times frank ectropion.

The following case is presented to illustrate a technique composed of a combination of these methods which seems to overcome these objections.

CASE REPORT

I. R. C., a 71-year-old white woman, was first seen in the McPherson Hospital in June, 1951, complaining of a mass in the right lower lid of six months' duration, which had recently increased rapidly in size. Examination revealed a firm, indurated mass, measuring 6.0 mm. by 10 mm., lying in the middle of the right lower lid firmly attached to the tarsus and skin (fig. 1).

Directly over the mass was a small fistulous tract extending down into it with some retraction of the lips of the orifice. A probe could be passed into the fistula and a small amount of mucus exuded from its orifice.

In spite of the presence of the fistula, the overlying skin did not appear inflamed and

* From the McPherson Hospital. Presented at the 11th clinical meeting of the Wilmer Residents Association.

the patient stated that at no time had there been any pain or inflammation. There was no regional adenopathy. Both globes appeared normal throughout, and corrected vision in each eye was 20/20.

The patient was seen in consultation by other members of the clinic, and all were in agreement that the lesion was probably malignant and should be treated by radical excision.

The following day, under infiltration anesthesia with two-percent procaine, the central two thirds of the lower lid was excised in a block dissection. The remaining lid was split on either side of the excised area and a small piece of skin and orbicularis was removed from the nasal portion of the remaining lid.

Fig. 1 (McPherson). Tumor lying in the middle third of the lower lid with mucus exuding from the fistula.

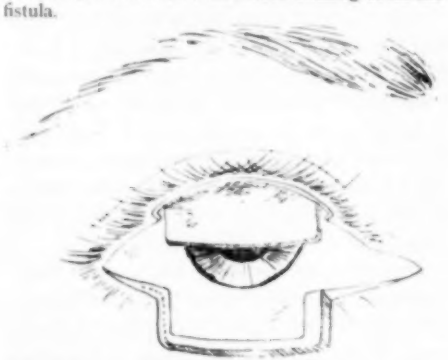

Fig. 2 (McPherson). Block dissection of middle two thirds of lower lid with halving on either side. Sliding tarsoconjunctival flap from upper lid.

The central portion of the upper lid was then halved in the manner described by Hughes, giving a sliding flap composed of tarsus and conjunctiva (fig. 2).

A mattress suture of 4-0 silk was passed through the shelf of tarsus remaining nasally in the lower lid, and the palpebral border of the sliding flap from the upper lid was then scarified. The flap was then brought into the defect below and sutured to the remains of the lower lid with buried gut sutures (fig. 3).

The remaining temporal portion of the lower lid was split at its palpebral border and this incision was extended through the outer canthus and up over the temporal region two cm. beyond the external canthus. A parallel incision was made 1.5 cm. below this, but slightly diverging from it.

At the temporal end of each incision re-

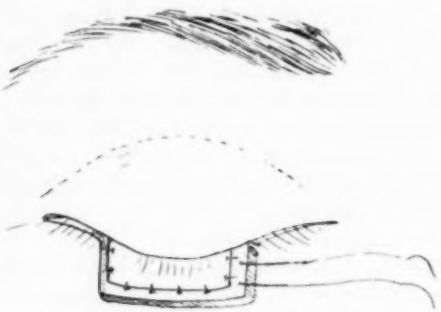

Fig. 3 (McPherson). Tarsoconjunctival flap sutured into defect in lower lid.

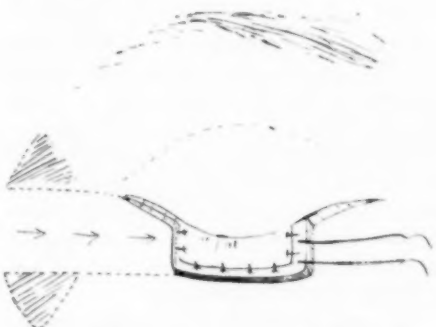

Fig. 4 (McPherson). Incisions in remainder of lower lid to create sliding skin flap. Relaxation triangles to be excised.

laxation skin triangles were excised (fig. 4). The skin flap was then slid over the newly formed tarsal plate as in the greater resection described by Reese. A single mattress suture of chromic catgut was passed through the base of the flap and secured to the orbital periosteum at the outer canthus to reduce tension at the skin edges.

The silk mattress suture previously placed in the tarsus of the lower lid nasally was brought through the tip of the sliding skin flap and tied over a rubber peg. The skin edges were approximated with interrupted sutures of 5-0 dermalon and the border of the skin above was sutured to the palpebral border of the upper lid (fig. 5). The lid was dressed with a pressure bandage.

Pathologic examination of the excised lid revealed a basal-cell carcinoma completely removed. Healing was uneventful and sutures were removed on the sixth postoperative day. The patient was discharged from the hospital on the eighth postoperative day and the lids were left closed for eight weeks (fig. 6).

At the end of that time, the lids were opened by a linear incision performed under infiltration anesthesia. To date, there has been no evidence of recurrence and the cosmetic result has been satisfactory (fig. 7).

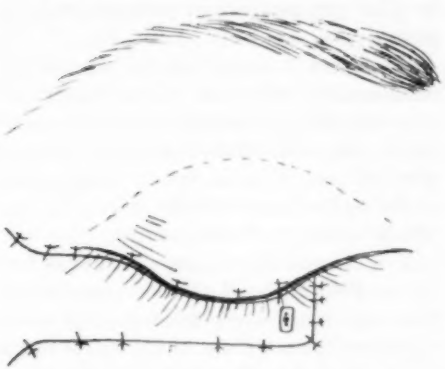

Fig. 5 (McPherson). Skin flap sutured in place over newly formed tarsal plate.

Fig. 6 (McPherson). Appearance of patient eight weeks postoperatively prior to opening of tarsorrhaphy.

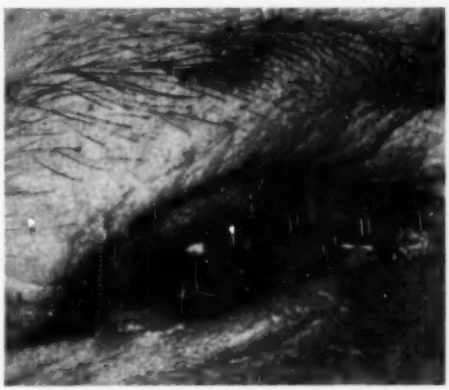

Fig. 7 (McPherson), Appearance of patient six months postoperatively.

Summary

A technique for reconstruction of the lower lid is presented which utilizes a sliding tarsoconjunctival flap from the upper lid and a sliding skin flap from the temporal region. In the case presented, it has afforded a satisfactory lower lid without the complications which have sometimes occurred with other techniques.

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OCULAR FINDINGS IN GOUT*

Report of a case of conjunctival tophi

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Historical

In the latter part of the 19th century gout was considered to be a very ubiquitous disease in general, and more specifically the etiologic agent of many and varied forms of ocular abnormality. Perhaps the greatest champion of gouty disease of the eye was Jonathan Hutchinson,[1-4] whose dynamic personality and eminent standing in the medical profession at that time assured widespread acceptance of any medical thought which he might advocate.

Hutchinson was probably the first to coin the term "hot eye" of gout and used it to describe a condition of the eye associated with quiet gout (referring to an absence of acute attacks of gout) in which the conjunctiva was injected, producing a hot and prickly feeling in the lids; this was often associated with some interference with the action of the ciliary muscle with resultant blurring of vision. The episodes were transient, lasting a very few days, and often were followed by manifest iridocyclitis.

He mentioned that the easily irritable and asthenopic eyes of young people were often associated with inherited gout. He also described a distinct clinical entity, a type of insidious but persistent and ultimately very destructive iridocyclitis in young people who themselves did not suffer from gout but who were direct descendants of parents with true gout. (In this regard a recent patient of Dr. F. B. Fralick[5] is of some interest. J. F. [#404779, University Hospital, Ann Arbor] has had 15 attacks of acute, nongranulomatous, exudative iridocyclitis. His father and grandfather both were proven gouty individuals, but the patient has not manifested any signs or symptoms of the disease as yet.)

This type of anterior uveal disease contrasted sharply with the acute, paroxysmal, highly inflammatory, and usually temporary iritis found in the truly gouty individual. Posterior synechias were slowly formed and followed by seclusion and occlusion of the pupil and with final phthisis bulbi or secondary glaucoma. The disease was ultimately bilateral and all forms of therapy were unsuccessful in staying the remorseless course of the disease.

Hutchinson believed that optic neuritis was often associated with gout and that a gouty diathesis was not infrequently responsible, in part at least, in the production of glaucoma. He described as "retinitis hemorrhagica," a condition in which edema of the optic disc and surrounding retina was associated with engorgement of the veins and hemorrhage into the retina, and went so far as to state that this type of retinopathy was (at least in older persons) almost pathognomonic of gout.

He reported several cases of corneal ulcer associated with gout which cleared rapidly with effective therapy of the latter condition. He differentiated between inherited gout and acquired gout, both as to the nature of the ocular disease and the type of therapy which proved most effective.

It is interesting to note that Doyne,[6] as late as 1910, reported what he considered to be a very rare form of iris pathology which he termed "guttate iritis" characterized by the presence of "small, warty, translucent excrescences on the pupillary margin of the iris." He found this condition only in people who were "obviously gouty" and considered it the "truest form of gouty iritis." From his description of the nodules, it would appear that he was referring to the Koeppe nodules which present-day knowledge ascribe to any

* From the Department of Ophthalmic Surgery, University of Michigan Medical School.

long-standing iridocyclitis of a quiet nature and more specifically to tubercular disease of the iris and, to a lesser extent, any granulomatous type of iritis.

From this brief discussion, it will be seen that the earlier writers believed gout to be an etiologic factor in practically every form of ocular disease. More recent authorities, however, among them Savin[7] and Wood,[8] are prone to doubt the true relationship between gout and the above conditions; as Savin puts it, the term "gout" was evidently used in a much broader sense in those earlier days. As medical knowledge has advanced in recent years it has become increasingly apparent that many, if not most, of the entities described above are in truth the result of entirely different causative agents.

Clinical picture

At present, the pendulum has apparently swung somewhat to the opposite extreme in that ocular manifestations of gout are seemingly rare. Thus Wood,[8] who is an authority on and has made a careful study of the subject, was able to find only four cases in a period of 15 years in which he was convinced that a true relationship existed between gout and associated ocular pathology. This may in part be due to the supposed fact that the incidence of gout is much reduced in modern times as compared to the much higher incidence of the disease in the latter part of the last century.

Many authorities, however, maintain that gout is as common today as it ever was, and that the infrequency of the disease is only an apparent condition, based primarily on the fact that the modern-day practitioner is for the most part unaware of its existence. Thus, in this disease as with so many other supposedly infrequent or rare diseases, the conclusion must be reached that, if the physician conscientiously looks for the disease, he will find it. With this thought in mind, a brief survey of the present-day accepted ocular manifestations of gout may be in order and of some value.

Gouty arthritic conjunctivitis

Duke-Elder[9] includes this entity as one of his types of conjunctivitis and defines it as "an inflammation of the conjunctiva without organismal infection, characterized by a marked hyperemia and a scanty discharge, and running an intractable and chronic course, associated with a gouty and arthritic diathesis." It is seen primarily in persons past middle age who are prone to excess in food and drink and whose ability to use or excrete the products of this intake is impaired.

The clinical picture is identical with that previously described by Hutchinson as the "hot eye of gout." The conjunctival vessels are unusually dilated and tortuous. The discharge is minimal or absent. The symptoms are inordinately annoying to the patient and consist of burning, hot, prickly, heavy feeling in the lids. Exacerbations of the condition are associated with dietary indiscretions and not infrequently with changes in the weather.

Local treatment, as in Hutchinson's day, is of little benefit and relief from the condition is best obtained by careful and persistent control of the systemic cause.

Scleritis and Episcleritis

Scleritis is a rare disease, but when present it is not infrequently associated with gout. The gouty variety may be either the anterior or the posterior type, the latter often being present concomitantly with tenonitis.

Episcleral involvement may be either of the nodular variety or, more frequently and classically, the so-called episcleritis periodica fugax. In the latter condition there is localized redness of the eye which lasts only a few days at most, appears typically at night, is not in itself painful, and characteristically disappears in one portion of the eye only to appear shortly thereafter in another quadrant of the same or opposite eye. Usually, the latent periods between the attacks are characterized by the complete lack of residual disease. Occasionally the involvement extends

from the episcleral tissues deep to the sclera, and there may then be associated uveal irritation.

In either the scleritis or episcleritis, deposits of urate crystals occasionally are found in the tissues.

Iridocyclitis

Iritis associated with gout is peculiar in its sudden onset (often at night), short but often stormy course lasting up to 10 days, rapid cessation, and the normal appearance of the eye between attacks. This picture is probably indicative of the chemical origin of the disease in contradistinction to a possible bacterial etiology.

If iritis is uncomplicated by other ocular involvement, the pain is usually minimal or absent. Quite frequently the iritis is of the gelatinous type, the anterior chamber being filled with a fibrinous type of exudate; this absorbs rapidly, however.

As already stated, the interval between attacks is usually remarkable in the absence of any residual signs, except possibly the presence of a few delicate posterior synechias. Not uncommonly some vitreous opacities are produced by the uveitis.

Commonly, the iritis is complicated by involvement of other ocular tissues with the resultant picture which will be described subsequently.

Tenonitis

Tenonitis does not occur alone, but always in association with scleritis. Tenonitis is characterized by severe pain, congestion, proptosis, and usually edema of the conjunctiva and lids.

Hot eye of gout

At the present time this term is often used when a combination of the factors already mentioned are present. Thus, iritis may occur coincidentally with scleritis and tenonitis. Not infrequently in these severe cases the intraocular pressure is elevated and the cornea becomes cloudy. Even in these very severe manifestations the course of the attack is remarkably short in most cases and the recovery almost complete. During the attack white precipitates may form in the anterior chamber which give a positive murexide test.

Keratitis

Wood[9] has reported marginal corneal ulcers associated with gouty attacks in the eye in which crystals thought to be urates were found. In all of these cases a definite increase in the uric acid content of the blood was present. A condition termed "keratitis urica" has been described in which crystals of urea and urates are laid down in the stroma of the cornea.

Duke-Elder[10] makes the point, however, that in this latter condition the uric acid level of the blood is normal and the patient does not have gout. He maintains that keratitis urica is a localized dystrophic disease of the cornea and not an inflammatory process associated with gout.

Deposition of urates

Tophi of the lids have occasionally been described. As has been described, uric-acid crystals have infrequently been demonstrated in the cornea and sclera as well as in the anterior chamber. Urates have never been found in the uveal tissue.

Sanyal,[11] in 1931, reported a unique case of a 12-year-old girl in whom concretions of calcium urate were periodically found in the conjunctival discharge. The optic discs were blurred and hyperemic and evidence of perivasculitis was present. The urine was found to contain large quantities of urate and uric-acid crystals. The diagnosis of gout could never be established in this patient.

An actual conglomeration of urate crystals into a definite mass comparable to tophus formation elsewhere in the body has apparently never been reported to my knowledge as occurring in the globe or associated conjunctiva. Subsequently in this paper a case report of conjunctival tophi will be presented.

Postoperative ocular gout

Berens[12] mentions the fact that an attack of ocular gout may be precipitated in a susceptible patient by cataract extraction. As early as 1840, Tyrrell[13] mentions the fact that rheumatism and gout may predispose to postoperative inflammatory disease of the eye.

In this regard it is interesting to note that the postoperative course of a recent patient of Dr. F. B. Fralick[14] was complicated by what apparently was an attack of this nature. The diagnosis of senile cataract had been made on J. G. (#655618, St. Joseph's Mercy Hospital, Ann Arbor, Michigan) and an extracapsular catract extraction without apparent complication was performed. All of the lens material excepting the posterior capsule was removed.

On the fourth postoperative day it was noted that the conjunctiva was markedly chemotic and on the fifth postoperative day a massive, fibrinous exudate was noted to be filling the anterior chamber and the pupillary opening. The eye was extremely painful.

The usual treatment for endophthalmitis was immediately instituted, although it was not thought that the condition was infective in origin. The possibility of an anaphylactic reaction to the lens protein was considered, but this was also thought unlikely due to the absence of any of the lens material save the posterior capsule.

A day or two after the appearance of the exudative reaction in the eye, it was ascertained that the patient had been suffering from a painful, large toe on the right foot for the preceding few days. A markedly elevated blood uric-acid level was found and the diagnosis of gout was established, the presence of which the patient had previously been unaware. The patient was placed on a regime of colchicine.

Although the original appearance of the eye was such that it was thought ultimate enucleation would be inevitable, the pathologic process gradually subsided over a period of about two weeks and, at the time of discharge from the hospital, the fibrinous exudate had entirely disappeared and the eye seemed well on the road to recovery. Unfortunately, a glaucomatous process appeared shortly afterward and, in spite of further surgery, the eye became stony hard and remained useless. In retrospect, it seemed most likely that the etiology of the inflammatory reaction was gouty in nature.

Pathology

Wood[9] has reported extensively on the pathologic findings associated with gouty disease of the eye. The sclera was markedly thickened, almost double its normal size, and heavily infiltrated with lymphocytes and plasma cells. On the posterior surface of one eye (clinically the patient had had recurrent attacks of tenonitis) were found several patches containing large numbers of small brown crystals which were thought to be urates. Unfortunately, however, chemical tests were not made prior to fixing the eye for microscopic study.

Large numbers of lymphocytes were found throughout the choroid, the ciliary body, and the base of the iris. However, few or none were found at the pupillary border of the iris, a fact which differentiates the pathologic picture in this disease from the usual type of iritis in which there is a marked inflammatory response at the pupillary border.

Only scant evidence of posterior synechias was present and there was no destruction of uveal tissue. The bacillary layer of the retina was damaged. The lens was clear. No cells were found in the aqueous, another fact which differentiates this disease from the usual type of iritis.

In general, Wood thought that the chemical irritant of gouty disease showed definite selective affinity for the sclera, choroid, and part of the retina while the iris and, to a lesser extent, the ciliary body were comparatively uninvolved.

Case report

Mr. A. W. (#191364) was first seen in the University Hospital in 1928 complaining

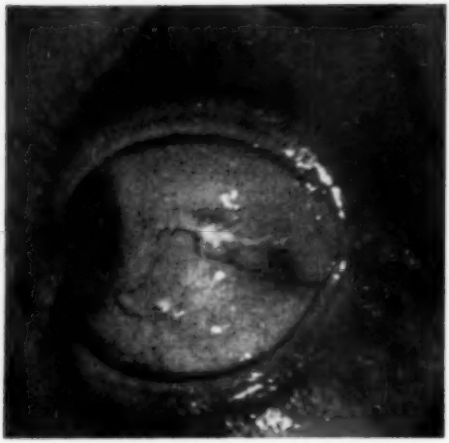

Fig. 1 (McWilliams). In the position normally occupied by the pinguecula, but lying on either side of the cornea, was a hard, white, chalky mass lying in the conjunctiva and apparently fixed to the episcleral tissue.

of occasional attacks of arthritis for the preceding five to six years. There was some enlargement of the phalangeal joints, but otherwise the examination was essentially normal. No cause for the arthritis could be found at that time and the diagnosis of chronic, infectious arthritis was made.

He was again seen in 1950 at which time he gave a history of nodular masses developing on his extremities over a period of a few years. Examination at that time revealed the presence of multiple nodular lesions over the upper and lower extremities varying from 1.0 to 10 cm. in diameter. Some of these were stony hard, some were soft and fluctuant, and several showed ulceration and secondary infection.

Serum uric acid was reported as 11.4 mg. percent.

Diagnoses were made of far advanced, gouty arthritis, renal insufficiency and anemia secondary to gout, organic heart disease, and questionable hyperthyroidism.

The patient was seen in the Department of Ophthalmology during his last hospital visit at which time the following findings were noted. The past history was negative for any ocular disease.

Uncorrected visual acuity was recorded as 6/6, O.U. A moderate degree of exophthalmos was present, the readings with the Hertel exophthalmometer at baseline 102 being 23.5 mm., O.D., and 24 mm., O.S. Both globes were easily reducible into the orbit and no evidence of exposure keratopathy was noted.

In the position normally occupied by the pinguecula, but lying on either side of the cornea, was seen a hard, white, chalky mass 1.0 to 2.0 mm. in diameter lying in the conjunctiva and apparently fixed to the episcleral tissue (fig. 1). No inflammatory reaction was present around the nodules and they had the appearance of large conjunctival concretions. Funduscopic examination was normal.

One of the small nodules was excised and microscopic examination of the fresh specimen revealed the presence of innumerable needlelike crystals characteristic of uric acid.

Diagnoses of exophthalmos and conjunctival tophi, O.U., were made. It was thought unlikely that the exophthalmos bore any direct relationship to the gout, although the possibility must be considered.

Summary

1. A brief historic review of gouty disease of the eye is presented.

2. The characteristic clinical picture of ocular gout is outlined. This includes conjunctivitis, scleritis, episcleritis, iridocyclitis, tenonitis, and rarely keratitis.

3. The possibility of postoperative inflammatory reaction following cataract extraction in the person with gout is stressed.

4. The typical pathologic picture is described.

5. A case of conjunctival tophi is presented.

Conclusion

In present-day clinical practice, gout is rarely considered in the search for an etiologic agent in ocular pathology. It is suggested that the incidence of gouty involvement of the eye is not so infrequent as mod-

ern belief would make it and that a knowledge of the ocular manifestations of the disease may be of some help in establishing the diagnosis when ocular gout is present.

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THE EFFECT OF INTRAVENOUS TYPHOID VACCINE ON ADRENAL CORTEX FUNCTION*

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The use of materials for their fever-producing properties has long had a place in medical therapeutics. Frankel,[1] in 1893, reported on the use of subcutaneous typhoid vaccine as a beneficial agent in the treatment of abdominal typhoid, and Rumpf[2] reported on equally beneficial effects produced by a pyocyaneus vaccine attributable to its pyrogenic properties.

"Protein-shock therapy" became very popular in the early part of this century, particularly in the treatment of arthritis and diseases of the eye. Foreign protein was first used in ophthalmology in 1915 by Schmidt[3] who gave milk injections to produce fever. Typhoid vaccine was first given intravenously by Kraus and Mazza,[4] in 1912, and was first used as a nonspecific protein by Miller and Lusk.[5]

Many investigators attempted to explain the mechanism whereby the agents employed bring about relief of symptoms, but were unable to reach a satisfactory explanation. Scully,[6] Gow,[7] Kibler and McBride,[8] and others recorded such changes as alterations in nitrogen excretion, white blood cell count, body weight, blood pressure, and body temperature after administration of these agents. An increase in normal serum complement and nonspecific serum antibodies was also reported.

Seibert,[9] in an exhaustive series of investigations, demonstrated that all the "injection fevers," whether due to vaccines, proteins, salts, and so forth, are due to a common pyrogenic factor which is heat-stable and passes bacterial filters. She also found that gram-negative bacilli are the most reliable pyrogen producers.

It is felt that all these agents contain bacterial products capable of producing fever, and, on the basis of many chemical investigations, the active agent would appear to be a polysaccharide. The pyrogenic agents isolated from B. typhosa[10,11] Ps. aeruginosa, and

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Proteus vulgaris[12] have been found to be carbohydrate in nature, and not protein. The use of the terms "nonspecific protein therapy" and "foreign-protein therapy" would thus appear to be founded on poor grounds. This work is well reviewed by Bennett and Beeson.[13]

The mechanism whereby typhoid vaccine and other pyrogenic agents beneficially affect ocular diseases has never been clear. Duke-Elder,[14] in 1934, wrote that injection of foreign proteins excites the immunity of the organism to renewed activity. He surmised that it was possible that the protein itself is not effective, but rather that the effective agent may be elaborated by the organism from it.

Hektoen,[29] in 1917, remarked that the use of antigenic materials could excite the elaboration in higher titers of antibodies to antigens to which the organism has previously been rendered sensitive. This so-called "anamnestic response" has also been recorded by Selye[21] as part of the response of the organism to stress.

Writing again in 1951, Duke-Elder[15] noted no advance in our knowledge of the fundamental mechanism whereby "protein shock" works.

Hambresin,[16] in 1940, wrote "the organism is undoubtedly stimulated, but the mode of such stimulation is unkown. Hyperleucocytosis, increase of antibodies, and rise in temperature have all been considered responsible, as have also activation of protoplasm, modification of permeability of blood vessels, stimulation of the infected tissues, and general colloidoclasis. It is probable that the reticulo-endothelial system plays a part in the mechanism of therapeutic shock. Many authorities consider histamine an important factor."

In 1947, Selinger[17] stated that "the basis for foreign-protein therapy is that the resultant increase in proteolytic and lipolytic enzymes in the blood aids in the destruction of bacteria, and in rendering their toxins harmless. At the same time the permeability of cells is said to be increased, so that antibodies can enter them more readily."

Von Szily[18] was able to demonstrate widespread inflammatory changes in the uveal tract of animals following milk injections, and concluded that these changes aid in clearing the inflammation.

Brown[19] noted interference by typhoid vaccine of experimental uveitis produced by bacterial and protein hypersensitivity, and an increase in the antibody content of the aqueous.

Cordes[20] wrote a comprehensive review of the status of fever therapy in 1944.

With the introduction of the "alarm reaction" and "adaptation syndrome" by Selye,[21] in 1946, the concept began to emerge that the pyrogenic agents owe their effect to the elicitation of an alarm reaction in the organism. The beneficial effect would then be expected to occur in the counter-shock phase, when there is an increase in the resistance of the organism.

Lewis and Page[22] reported in 1948 that both normal and adrenalectomized rats receiving replacement of Compound A or adrenal cortical extract demonstrated, after receiving typhoid vaccine, a fall in blood lymphocytes and a leukocytosis. The animals not receiving hormone replacement showed the same response in lymphocytes, but a lesser increase in polymorphonuclear cells.

Sayers and Sayers[23] demonstrated in 1949 that killed typhoid organisms produce histologic changes in the adrenal cortex of animals characteristic of the general response to stress.

Altschule, Parkhurst, and Promisel[24] followed the eosinophil counts, lymphocyte counts, and 17-ketosteroid urinary output in patients receiving typhoid vaccine for the treatment of psychoses. They noted a fall of the blood lymphocyte and eosinophil level, and an irregular increase in the urinary uric acid to creatinene ratio. There was no consistent effect on the urinary ketosteroid output. They concluded that apart, at least, of the effect produced by typhoid vaccine is due to activation of the adrenal cortex, although

they feel that other factors of toxic or immunologic nature may play a role.

Olson, Steffensen, Margulis, Smith, and Whitney[25, 26] employed ACTH and cortisone in the treatment of inflammatory diseases of the eye on the basis that foreign protein probably stimulates the release of endogenous adrenocorticotropic hormone, with subsequent activation of the adrenal cortex to increased activity. They wished to see whether the therapeutic response to these agents is comparable to that obtained with foreign protein.

Arendshorst and Falls[27] followed the eosinophil response in patients given typhoid vaccine intravenously, and noted an eosinopenia proportional to the degree of fever produced. These authors state that if there is no eosinopenia, there is no therapeutic benefit.

The purpose of this presenttaion is to report observations made on six patients receiving typhoid-paratyphoid vaccine for the treatment of various ophthalmic conditions. No attempt has been made to correlate the physiologic changes induced with therapeutic benefit to the patient.

During a control period of 48 hours, measurements were made of total excretion of 17-ketosteroids, direct eosinophil counts, white blood cell counts, blood pressure, weight, fluid intake and output, and in three of the cases total uric acid and creatinine urinary output.

These same measurements were then repeated in succeeding 24-hour periods after the institution of treatment with typhoid-paratyphoid vaccine, given intravenously in doses varying from 10 to 400 million killed typhoid organisms. Eosinophil counts were measured both before and four hours after the injection, using the Harriet Lane method of direct counting, which is a modification of the method reported by Klein and Hanson.[30]

In one patient only, 11-oxysteroid excretions were measured. Not all studies were carried out on all patients.

The results of these studies in the individual patients are shown in Tables 1 to 6. They may be summarized as follows:

1. *17-ketosteroid excretion.* In all but one patient a marked increase in the 24-hour output of 17-ketosteroids occurred in the period following the injection of typhoid vaccine, as compared with the control period. In Case 1 the output was almost trebled (table 7).

2. *11-oxysteroid excretion.* In the one instance where tested, a notable increase in the 11-oxysteroid output was found, the excretion in one period being more than seven times that in the control period (table 7).

3. *Blood cytology.* An invariable and marked decrease in the circulating eosinophil level occurred in all cases, which was observed at four hours, and persisted at least 24 hours. In almost all cases the reduction was sharp, and very often no circulating eosinophils could be found (table 8).

4. *Uric-acid excretion.* Two of the cases studied demonstrated an increase uric-acid excretion as compared with the control period. In no instance was the uric acid to creatinine ratio significantly altered. No conclusions can be drawn from this, since the dietary intake was not kept constant (table 9).

5. *The fluid balance* in the face of typhoid vaccine administration was greatly variable. Case 3 demonstrated a relative retention of fluid on the day typhoid vaccine was given (table 10).

6. *No significant alteration* occurred in the body weight or in the blood pressure.

Conclusions

The above results, particularly the eosinophil response, and the urinary 17-ketosteroid and 11-oxysteroid outputs are strongly suggestive of an overaction of the adrenal cortex as a part of the general biologic response to the pyrogenic agent (typhoid vaccine). These observed effects are similar in nature and degree to those induced by administration of adrenocorticotropic hormone or cortisone.[28]

It seems clear, therefore, that in addition to

TABLE 1. Mrs. E. E. (JHH 546546) Granulomatous iridocyclitis

Date	Dose Typhoid Vaccine	Max. Temp.	Direct Eosin. Count	17-Keto-steroids (mg./24 hr.)	11 Oxy-steroids (mg./24 hr.)	Uric Acid (mg./24 hr.)	Creatinine (mg./24 hr.)	Uric Acid / Creatinine	Fluid Intake	Urine Output	Output / Intake	Weight (pounds)
10/19		98.6	133.3									118.5
10/20		99.6							3500	3300	0.9	
10/21		99.0		4.0	0.37				3840	2925	0.8	
10/22		98.6		3.8	0.17	402.5	796.38	0.5	3788	2125	0.6	
10/23		99.4	133.3			454.6	748.9	0.59	2250	2050	0.9	120
10/24	20×10^6	100.4	222.2	11.8	1.25	451.5	694.4	0.66	1500	2080	1.3	120
10/25	60×10^6	103.0	22.2			130.95	346.3	0.28	2250	1800	0.8	
4 hr. later			0									
10/26		99.4				535.5	1049.6	0.50	2250	1800	0.8	
10/27		99.2	244.4						2640	1250	0.4	
10/28	60×10^6	105.0				239.2	540.9	0.48	2910	3050	1.1	116
10/29		99.6							2970	400	0.15	118
10/30	60×10^6	102.0	111.1	11.2	0.43				3085	1800	0.45	
10/31		99.1	0			191.2	426.6	0.26	2890	1675	0.4	
11/1	75×10^6	100.2	111.1			320.0	834.0	0.39	2350	2200	0.95	
11/2		99.2	88.8			441.0	777.0	0.55	3830	1250	0.3	
11/3	75×10^6	100.8	44.4						3230	3025	0.95	
11/4		98.6	22.2									
11/6		98.0	200.0									

TABLE 2. Mrs. M. T. (JHH 538458) Granulomatous choroiditis

Date	Dose Typhoid Vaccine	Max. Temp.	WBC.	Direct Eosin. Count	Polys. (percent)	Lympho. (percent)	17-Keto-steroids (mg./24 hr.)	Uric Acid (mg./24 hr.)	Average Blood Pressure	Fluid Intake	Urine Output	Output / Intake	Weight (pounds)
1/9		99.0	5,600										132
1/10		99.0							115/75				132
1/11		99.8					4.9	415	119/78	4390	2200	0.5	133
1/12		99.8	4,400	166.6	62	21	4.9	415	110/76	4700	4850	1.0	134
1/13	50×10^6	106.2	4,450	166.6	57	33	12.6	573.9	120/80	1430	2050	0.9	132
4 hr. later				0									
1/14		99.0	14,450	0					110/70	3475	1150	03.	
1/15	80×10^6	104.2	8,800	66.6	62	62			160/110	3430	1675	0.5	
4 hr. later				0									
1/16		99.8	14,600	0	89	10			106/72	4000	750	0.2	130
1/17	125×10^6	104.4	8,000	133.3	72	23	14.1	1249.8	152/96	1890	1625	0.8	131
4 hr. later				22.2									
1/18		99.0	9,000	66.6	76	17			130/90				129
1/19	200×10^6	101.6	6,250	88.8	69	28			120/70				129
4 hr. later				44.4									
1/20		99.0	4,750	0	67	28			100/80				128
1/21	400×10^6	102.2	16,400	0	84	12	12.49	477.5	106/68				127
1/22		98.0	11,850	22.2	87	12							126

TABLE 3

MR. F. H. (JHH 305450) CHRONIC GRANULOMATOUS UVEITIS

Date	Dose Typhoid Vaccine	Max. Temp.	Direct Eosin. Count	17-Keto-steroids (mg./24 hr.)	Uric Acid (mg./24 hr.)	Creatinine (mg./24 hr.)	Uric Acid / Creatinine	Fluid Intake	Urine Output	Output / Intake	Average Blood Pressure	Weight (pounds)
2/12		98.8	166.6								110/75	150
2/13		98.0						4009	2400	0.6	110/65	150
2/14		98.6	244.4	12.1	257.6	573.44	0.45	3620	3150	0.88	110/65	149
2/15		98.6		12.1	257.6	573.44	0.45	6240	4500	0.56	110/68	151
2/16		98.6	222.2					3080	4300	0.72	108/74	147
2/17	10×10^6	102.4	444.4	18.5	217.6	696.32	0.31	4860	1350	0.29	108/76	146
2/18		100.0	66.6					4220	2575	0.6	95/68	
2/19	25×10^6	103.0	333.3	13.9	232.5	700.0	0.37	3160	700	0.22	105/68	
4 hr. later			22.2									
2/20		99.6	115.5									

TABLE 4

MR. T. C. (JHH 170674) RECURRENT NONGRANULOMATOUS IRITIS WITH MARIE-STRUMPELL SPONDYLITIS

Date	Dose Typhoid Vaccine	Max. Temp.	Direct Eosin. Count	17-Keto-steroids (mg./24 hr.)	Uric Acid (mg./24 hr.)	Creatinine (mg./24 hr.)	Uric Acid / Creatinine	Fluid Intake	Urine Output	Output / Intake	Weight (pounds)
11/1		98.6									99
11/2		98.6	22.2	2.37	310.6	364.0	0.85	2810	550	0.2	
11/3		98.6		2.37	310.6	364.0	0.85	2640	325	0.2	
11/4		98.6	122.2					2590	1100	0.4	97
11/5	20×10^6	101.6	66.6	5.4	500.0	657.7	0.76	2100	1250	0.55	97
4 hr. later			0								
11/6		100.0	11.1					3030	625	0.2	95
11/7	30×10^6	102.4	177.7	4.4	525.0	625.5	0.85	2270	1500	0.67	96
4 hr. later			22.2								
11/8		98.0	22.2					2850	200	0.08	95

their other effects on the organism, typhoid vaccine and allied pyrogens activate the adrenal cortex. Whether this occurs through stimulation of the anterior pituitary gland to production of adrenocorticotropic hormone, or by direct stimulation of the adrenal cortex is unanswered by this study.

It is possible, though by no means proved, that the activation of the adrenal cortex is responsible for the therapeutic effect of "foreign proteins." The successful use of cortisone and ACTH in disease conditions would strongly suggest that the release of endogenous adrenocorticotropic hormone and cortisone under the influence of these materials is an important factor. One must still keep in mind the possibility that this is but another manifestation of what has been termed by Woods[31] the biologic reorientation which follows the use of fever-producing agents.

Further studies in patients receiving these agents, and animal experimentation are needed before we can adequately evaluate the fundamental mechanisms by which pyrogenic agents influence clinical lesions.

TABLE 5

MR. H. M. (JHH 437949) CORNEAL LACERATION

Date	Dose Typhoid Vaccine	Max. Temp.	Direct Eosin. Count	17-Ketosteroids (mg./24 hr.)
8/13		99.0		8.07
8/14		98.6	177.7	8.07
8/15	10×10^6	100.6	222.2	7.5
4 hr. later			111.1	
8/16		99.6	66.6	
8/17		98.6	177.7	

SUMMARY

A brief review of postulated mechanisms of action of pyrogens is presented, and the evolution of the concept of action through activation of the adrenal cortex is traced. Results of studies on six patients are presented, and these are interpreted as indicative of adrenal cortical stimulation by the agent employed.

The Johns Hopkins Hospital (5).

TABLE 6

MR. F. M. (JHH 589425) NONGRANULOMATOUS IRIDOCYCLITIS, RECURRENT

Date	Dose Typhoid Vaccine	Max. Temp.	Direct Eosin Count	17-Ketosteroids (mg./24 hr.)	Fluid Intake	Urine Output	Output / Intake	Weight (pounds)
11/9		99.0	188.8	14.9	3710	1500	0.4	206
11/10		98.6		14.9	2960	1125	0.38	206
11/11	25×10^6	103.0	111.1	18.6	2000	750	0.375	204.25
4 hr. later			222.2					
11/12		101.1	44.4		3160	500	0.16	201.50
11/13			111.1					203.75

TABLE 7

17-KETOSTEROID OUTPUT (mg. per 24 hr.)

Case No.	Control Period	First	Second	Third	Fourth	Fifth
1	3.9	11.8			11.2	
2	4.9	12.6		14.1		12.49
3	12.1	18.5	13.9			
4	2.37	5.4	4.4			
5	8.07	7.5				
6	14.9	18.6				

11-OXYSTEROID OUTPUT (mg. per 24 hr.)

Case No.	Control Period	First	Fourth
1	0.27	1.25	0.43

TABLE 8

DIRECT EOSINOPHIL COUNTS (cells per cmm.)

Case No.		First	Second	Third	Fourth	Fifth	Sixth
1	Before	222.2	22.2		111.1	111.1	44.4
	4 hr. after		0				
	24 hr. after				0	88.8	22.2
2	Before	166.6	66.6	133.3	88.8	0	
	4 hr. after	0	0	22.2	44.4		
	24 hr. after	0	0	66.6	0	22.2	
3	Before	444.4	333.3				
	4 hr. after	111.1	22.2				
	24 hr. after	66.6	155.5				
4	Before	66.6	177.7				
	4 hr. after	0	22.2				
	24 hr. after	11.1	22.2				
5	Before	222.2					
	4 hr. after	111.1					
	24 hr. after	66.6					
6	Before	111.1					
	4 hr. after	22.2					
	24 hr. after	44.4					

TABLE 9

URIC ACID AND CREATININE OUTPUT; URIC ACID TO CREATININE RATIO

Case No.		Control Period	First	Second	Third	Fourth	Fifth
1	Uric Acid	402.5	451.5	130.95	239.2		320.0
	Creatinine	796.4	694.4	346.3	540.9		834.0
	U:C Ratio	0.5	0.6	0.28	0.48		0.39
2	Uric Acid	415.0	573.9		1249.8		477.5
	Creatinine						
	U:C Ratio						
3	Uric Acid	257.6	217.6		232.5		
	Creatinine	573.4	696.3		700.0		
	U:C Ratio	0.45	0.31		0.37		
4	Uric Acid	310.6	500.0	525.0			
	Creatinine	364.0	657.5	625.5			
	U:C Ratio	0.85	0.76	0.85			

TABLE 10

URINE OUTPUT TO FLUID INTAKE RATIO

Case No.	Control Period	First	Second	Third	Fourth	Fifth	Sixth
1	0.8	1.3	0.8	1.1	0.45	0.95	0.95
2	0.75	0.9	0.5	0.8			
3	0.7	0.29	0.22				
4	0.3	0.55	0.67				
5	0.39	0.37					
6							

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THE DIAGNOSIS OF OCULAR TUMORS OF VARIOUS TYPES*

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A statistical analysis of 170 consecutive ocular tumors, as they appeared over a period of 10 years, was presented in March, 1951, before the Third Annual Clinical Conference of the Wills Eye Hospital. This statistical study of incidence and mortality rates has been published.[1] No attempt was made at the time of that presentation to discuss diagnosis or treatment. A third and subsequent paper will discuss treatment.

This paper, at this time, has as its purpose a further consideration of these varied orbital tumors in terms of gross pathology, hence, diagnosis. All the cases included in the study were either operated by me or by my senior associates, or X-ray and radium therapy was directed by me. Cases seen in consultation and cases not treated by me are not included herein.

In presenting these cases, incidence and mortality rates will be shown very briefly as abstracts from the original tables. The incidence of mortality in some of these tables will certainly change over the years to come. The mortality rates listed are for the present.

At least two more of the patients with carcinoma of the lacrimal sac (of the four cases to be discussed) will succumb before many more years. One patient died after three years, two are still alive, and one case is still too recent for any prognosis except that of graveness. This illustrates what is meant by the statement that change in the mortality rates is certain to occur in the future in cases in which any of these various types of tumors are malignant.

No attempt is made to discuss differential diagnosis. Much has been written about this in the past and much is still to be written. Differential diagnosis, a subject which might in the future be proper to discuss together with treatment, is not relevant to this paper. Applicable here, however, is mention of a dislike for partial removal—that is for preliminary biopsy. Complete removal of the tumor is the best for proper study.

The pathologists at the Graduate Hospital of The University of Pennsylvania, Jeane's Hospital, and the Wills Eye Hospital made the diagnoses in all instances except in less than 10 cases. In these individual instances diagnoses were confirmed at other institutions at the request of the pathologist concerned. Among these were the following cases: one case of reticulum-cell sarcoma; one of hypernephroma; one of lymphoblastoma; one of follicular lymphoma; and one of malignant melanoma, with little pigment, of the lower lid. This case will be discussed more in detail later.

There is still disagreement concerning the diagnosis in one case of possible mixed-cell tumor of the lacrimal gland; the pathologist considers the pathologic findings more like the inflammatory ones of a chronic adenitis rather than mixed-cell tumor of the lacrimal gland. This case is included in the analysis as malignant. The future may show this to be an error. I am greatly indebted to my colleagues for their expression of confidence in referring many of these cases.

In this presentation, no attempt has been made to classify the various cases of intraocular melanomas into the various subdivisions discussed and explained by Ash and Wilder.

The 33 cases of malignant melanomas, making up 20 percent of all cases, had a known mortality rate of 16 percent; 68 percent were intraocular cases, and 32 percent were extraocular. Seventeen of the cases were intraocular (retinal or choroidal) and among these, up to the present time, there have been three deaths.

* From the Wills Eye Hospital and the Graduate Hospital of the University of Pennsylvania. Presented before the Eastern Sectional Meeting of The American College of Surgeons, Atlantic City, February 12, 1952.

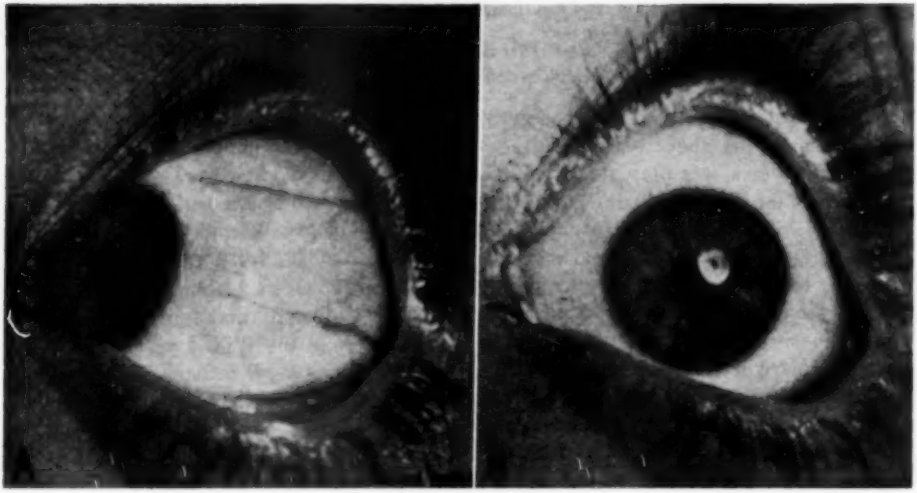


Fig. 1 (Spaeth). Malignant melanoma of the iris.

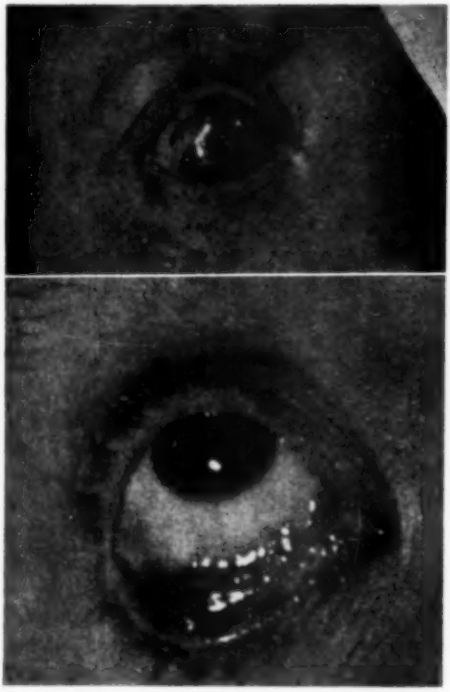


Fig. 2 (Spaeth). Malignant melanosis, superior conjunctival cul-de-sac; inferior conjunctiva cul-de-sac.

Of the 11 extraocular cases, one, a non-pigmented melanoma of the lower lid, was operated in another city and was diagnosed at an internationally known laboratory of pathology as a basal-cell carcinoma. Because of this the patient, a physician, was given massive X-ray therapy. When recurrence two years later necessitated the complete removal of the lower lid, a correct diagnosis was made at the same institution by comparing the tissue from the earlier biopsy with that of the diseased lower lid.

The point of importance in this case is, of course, that unnecessary and unwise X-ray therapy followed the first surgery because of the mistake in diagnosis. The error made in diagnosis is mentioned here to emphasize the difficulty in making a correct diagnosis when a melanoma is sparsely pigmented.

Of the other 11 cases of extraocular malignant melanomas, one developed in long-standing melanosis and the others were marginal (the lids), limbal, and/or conjunctival. Up to the present time there have been two deaths in this group, both by metastases to the liver.

Of the four cases of malignant melanoma

of the iris included herein, one, referred by a colleague, has already been published[2] (fig. 1). In one instance, a case operated in another city, confirmation of the diagnosis has never been received.

Two of the five cases of malignant melanomas of the conjunctiva were of classical malignant precancerous melanosis (fig. 2), as first outlined by Reese.[3] One case was of malignant melanosis of the superior conjunctival cul-de-sac, and one was malignant melanosis of the lower conjunctival cul-de-sac. Two of these five patients have died up to the present time.

Of the 17 patients reported by Reese, at least seven had died from five to 10 years after initial appearance. This is a much longer period of observation than for my cases. However, as stated earlier, mortality rates in this series of cases are certain to change in the years to come.

It is relevant to call attention to a statement by Reese that irradiation in these cases, in the precancerous stage, gives excellent results. He felt that any temporizing procedures in these instances may lead to fatal consequences.

Some cases of benign melanomas were seen but were not included in the total of malignancies. Difficulty in diagnosis is illustrated by two cases presented here. The melanoma shown in Figure 3 was increasing in size and was therefore operated. The tumor was resected and was skin-grafted satisfactorily. After careful tissue study, the growth was considered a benign melanoma and the clinical course of the case in the past three years has seemed to confirm this.

Figure 4 shows a so-called melanoma of the iris which increased in size over the years; when examined microscopically, it proved to be of a benign type, and hence is not listed as malignant.

Figure 5 is the microscopic slide of a case of malignant melanoma (see fig. 6) which had perforated the sclera, appearing extraocularly as seen in the illustration and in the histologic specimen.

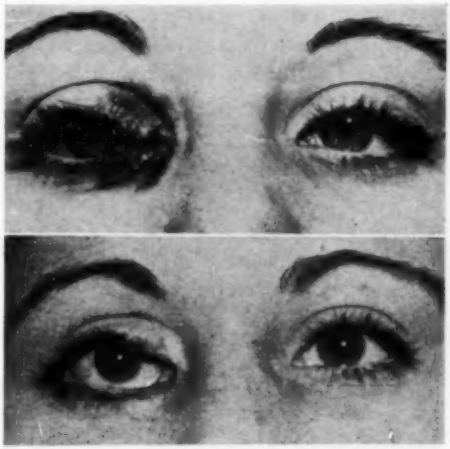


Fig. 3 (Spaeth). Melanosis. Histologic examination showed no precancerous changes.

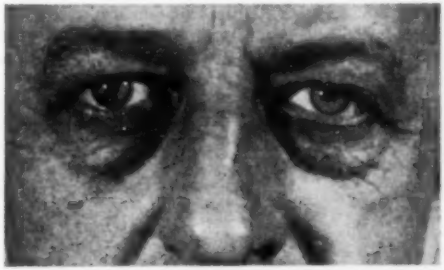


Fig. 4 (Spaeth). Melanoma of iris, increasing in size, when examined microscopically showed no precancerous changes.

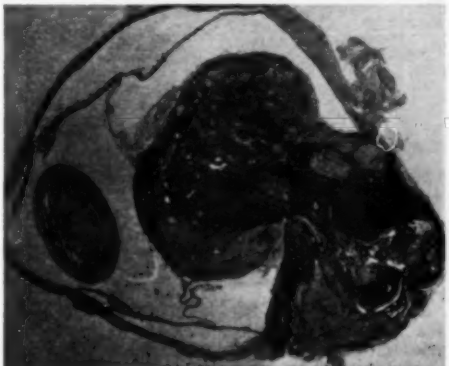


Fig. 5 (Spaeth). Intraocular malignant melanoma. Section shows perforation through the sclera.

Tumors of the nervous system include 10 cases of neurofibroma of the orbit and/or the lids. The tumors of neurogenic origin include 15 percent of all cases of ocular malignancy, and 5.6 percent of these cases were retinoblastomas.

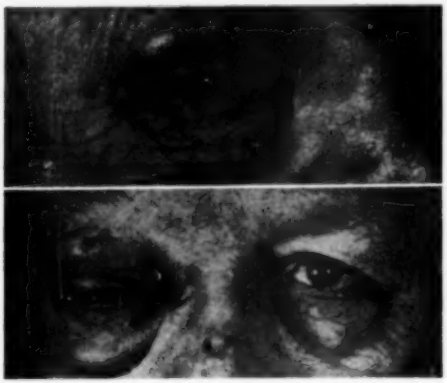


Fig. 6 (Spaeth). Intraocular malignant melanoma. The sharp inflammatory reaction was the result of a perforation of the sclera.

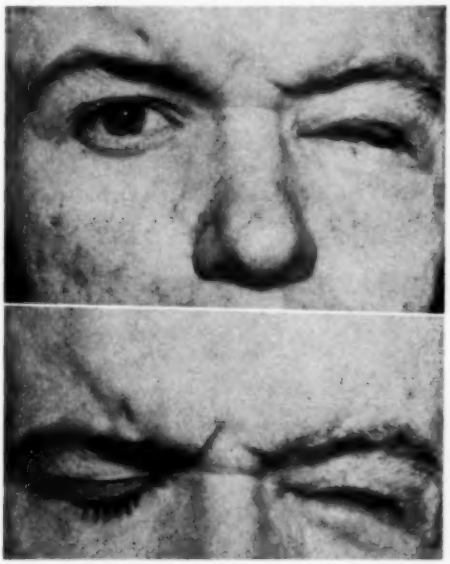


Fig. 7 (Spaeth). Neurofibroma of the orbit and the zygomatic region operated 10 years earlier; now sarcomatous invasion. Attention was called to this by a sudden massive hemorrhage with swelling into the soft tissues of the left side of the face and the neck. Condition as illustrated after further resection and X-ray therapy.

Figure 7 illustrates a case of neurofibroma in which sarcoma developed 10 years after the initial surgery. This is not too rare a complication, though difficult to reconcile.

Figure 8 depicts a case (seven years earlier) of neurofibroma of the sheath of Schwann of the fifth nerve. Figure 9 is one of meningioma of the sheath of the optic nerve. In Figure 10 are drawings of this retrobulbar growth, showing the perineural growth. Figure 11 is a neurofibroma (pachydermatocele) of the orbit and of the lids.

There were three cases of neurofibroma of the optic nerve. These three cases and the 10 other cases of varied neurofibromatoses should probably be listed together. Their histologic differentiation—that is, von Recklinghausen's disease, schwannoma,

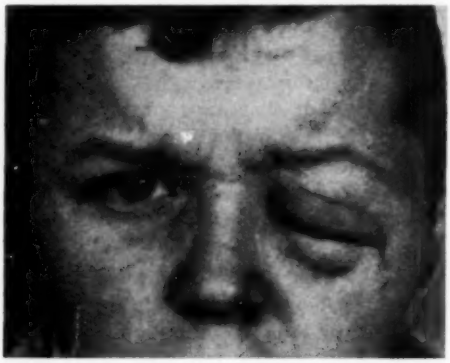


Fig. 8 (Spaeth). Neurofibroma of sheath of Schwann, fifth nerve.

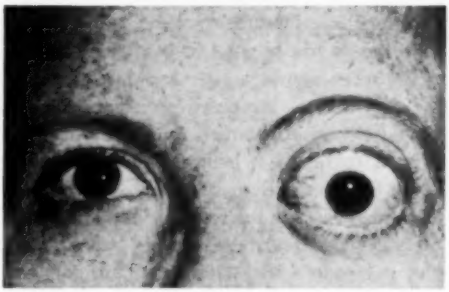
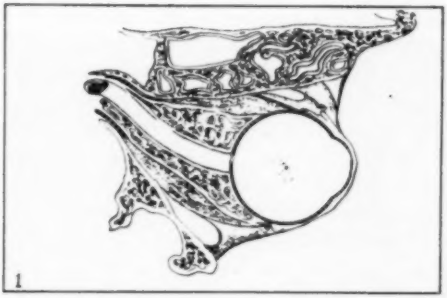


Fig. 9 (Spaeth). Exophthalmos from retrobulbar meningioma of the sheath of the optic nerve.

neurogenic fibroma, and so forth—is not to be discussed here.

Figure 12 is a remarkable case of bilateral neurofibroma of the infraorbital nerves in the two orbits. The first tumor appeared in the left eye and was successfully removed. The second tumor appeared a year later in the right eye and was also removed with success.

Two of the cases of neurofibromatosis had a most interesting family history. A grandfather died of an intracranial neurofibroma, his daughter had a marked case of generalized neurofibromatosis, and his granddaughter had a similar situation, though to a lesser degree. Figure 13 shows the granddaughter's cafe-au-lait spots and one small nodule. These cases were presented at the Section of Ophthalmology of the College of Physicians by Dr. Edith Harvey[4] seven years ago.



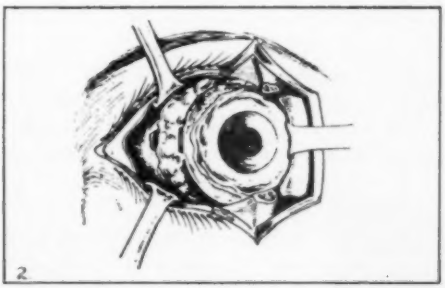


Fig. 10 (Spaeth). (1) Drawing illustrating side view of meningioma embracing the optic nerve. (2) Front view illustrates the manner in which the eyeball rested upon this neoplasm.

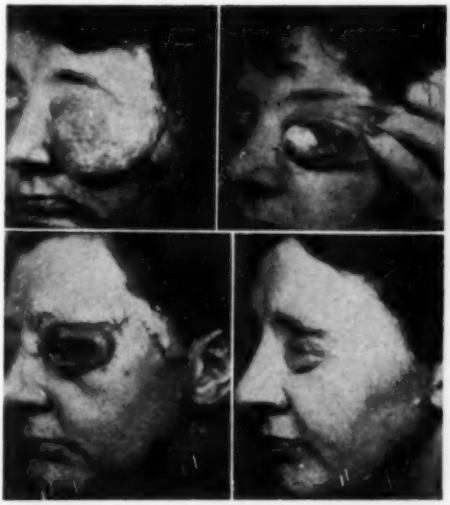


Fig. 11 (Spaeth). Neurofibroma of the orbit and the lids. Radical surgery—removal of all structures in the orbit, including remains of the roof of the orbit. Lid margins were sutured with permanent intermarginal adhesions to protect the exposed dura.

The case of plexiform neurofibroma reported herein, and operated through a Krönlein approach, had been previously explored, one year before, in Germany and the patient had been informed that she had no tumor.

Two of the nine cases of retinoblastoma seen were bilateral, and seven were unilateral. There was one death in this group. It was a unilateral case. There were differences in opinion among several ophthalmologists as to gross (macroscopic) diagnosis. No ocular surgery was done. The child died from intracranial retinoblastoma metastases.

It is interesting that no other case of retinoblastoma had intracranial extensions.

I am not too impressed with the necessity for a transfrontal exploratory craniotomy in these instances unless a section of the optic nerve shows tumor cells within the nerve itself. There was one such instance. This case was treated, however, with massive X-ray therapy and the patient has since developed into normal adolescence, and will

rather likely continue to develop normally in the future.

One similar additional case, not included herein, was in the practice of one of my associates, Dr. William E. Krewson, III. This also was treated successfully with X-ray therapy.

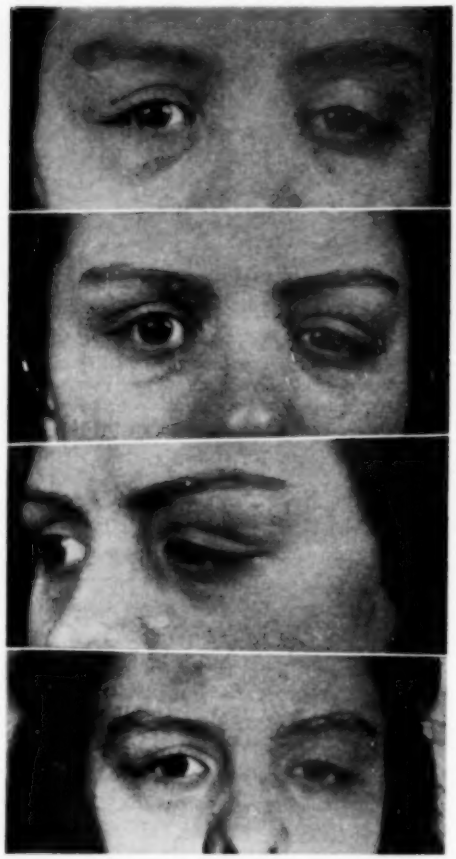


Fig. 12 (Spaeth). Neurofibroma of the infra-orbital nerves, first appearance on left, second tumor on right a year later.

One case of bilateral retinoblastoma was treated unsuccessfully, unilaterally, with radon seeds. The other bilateral case herein reported was, at the time of enucleation of the first eye, diagnosed by the pathologist as a pseudoglioma. The diagnosis of this was changed, however, following the examination of the second eye after its enucleation. There was so much necrosis in the first eye that the error in diagnosis was quite possible.

In the analysis of the sarcomas are included tumors of the lymph and blood-vessel systems. Tumors of the lymph cells, 11 cases, constituted 6.1 percent of all malignancies; hemangiomas, 10 cases, constituted six percent of all malignancies; and sarcomas, 25 cases, were 15 percent of all malignancies. The mortality rate of the sarcomas was 30 percent. Cases of Hodgkin's disease, of myelogenous leukemia, and similar conditions, are not included in this analysis.

Eleven of the cases in this group were lymph-cell tumors. One case was a follicular lymphoma which responded at first to nitrogen mustard. A second recurrence had a similar result. Now, two years later, the patient is in the hospital with another recurrence, this time with a poor prognosis.

Two of the eight cases of lymphosarcoma were so-called reticulum-cell sarcoma. Figure 14 shows one such case, which responded beautifully to X-ray therapy. Six cases of lymphosarcomas were not reticulum cell in type (fig. 15).

Hemangiomas were seen in 10 cases. This subdivision includes only hemangiomas which were nodular masses (figs. 16 and 17). Nevus flammeus and other capillary hemangiomas, strawberry marks, and similar skin blemishes were not included herein; in one such case, however (fig. 18), a

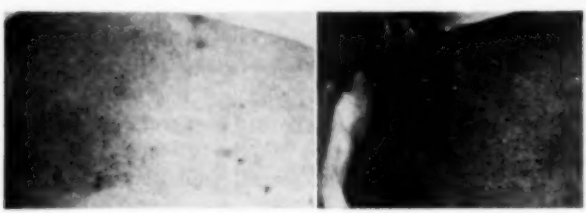


Fig. 13 (Spaeth). Cafe-au-lait spots and one small nodule of von Recklinghausen's disease.

basal-cell carcinoma developed three years after removal of the initial growth.

Another hemangioma of the conjunctiva, when resected, was considered by different pathologists to be either a hemangioma or malignant melanosis (fig. 19); clinically, however, this tumor was a hemangioma.

Of the remaining 25 cases of sarcomas in this group, one was a classical giant-cell sarcoma. This started in the medial wall of the orbit and was seen first by a rhinologist. The surgical treatment instigated was applied with such timidity that the case was transferred to the eye service for the necessary surgery.

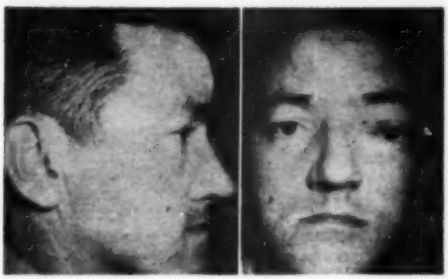


Fig. 14 (Spaeth). Reticulum cell sarcoma.

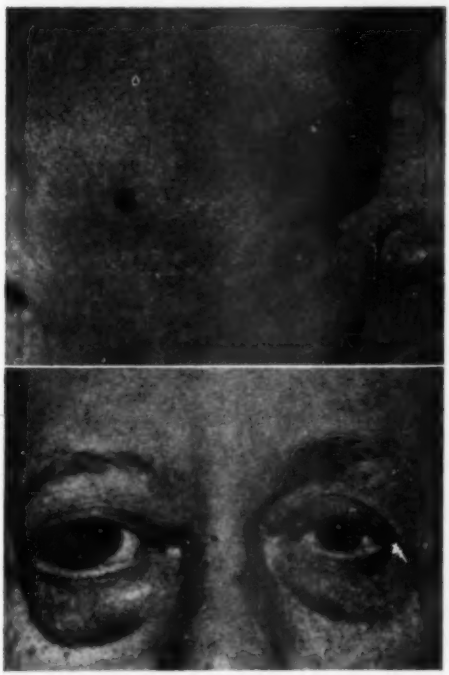


Fig. 15 (Spaeth). Lymphosarcoma, retrobulbar.

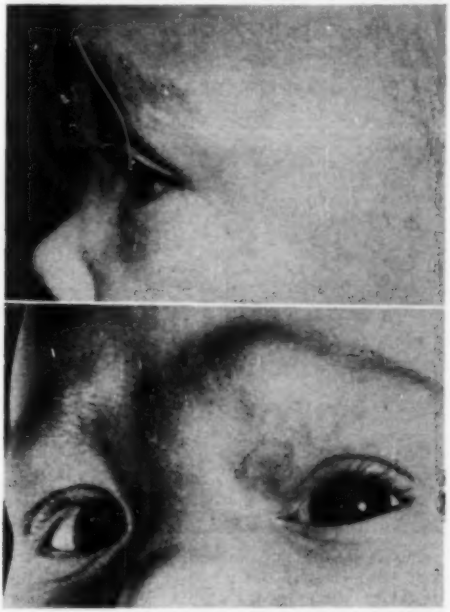


Fig. 16 (Spaeth). Hemangioma in an infant.

Fig. 17 (Spaeth). Hemangioma in an infant.

Fig. 18 (Spaeth). Capillary hemangioma which subsequently developed carcinomatosis.

Fig. 19 (Spaeth). Limbal hemangioma simulating melanosis.

Fig. 20 (Spaeth). Giant-cell sarcomas at time of first visit. Exophthalmos with the bony deformity of the maxilla.

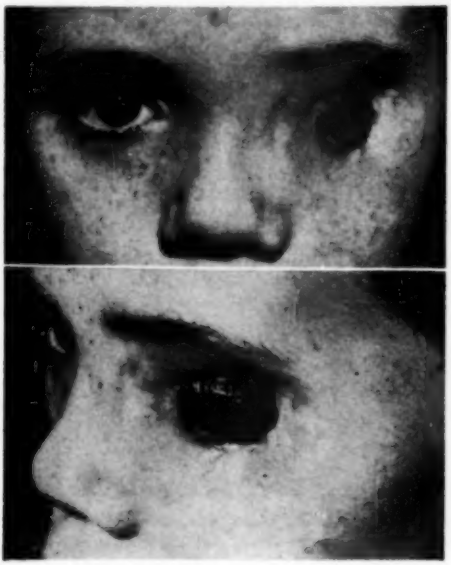


Figure 20 was made at the time of the first examination in this case; Figure 21 shows a recurrence two years later. Figure 22 shows the same patient, now in late adolescence, wearing a prosthesis which, although not too satisfactory, is still fairly good. (The photograph had been retouched by the photographer prior to its receipt. Not too hei-

Fig. 22 (Spaeth). Condition at present with complete recovery. Defect and the prosthesis patient is wearing.

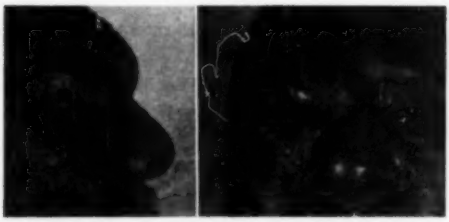


Fig. 23 (Spaeth). Osteogenic sarcoma of the supraorbital ridge.

Fig. 24 (Spaeth). Osteogenic sarcoma, after initial orbitotomy of the orbit.

Fig. 21 (Spaeth). Recurrence at the operative site two years later.

nous an act!) It also shows the patient, at the present time, without this prosthesis.

Two cases of sarcomas were intraocular and metastatic, while one case (not a melanoma) was apparently primary within the globe. Sixteen cases were retrobulbar. There were three deaths in this group, two of them in children below the age of five years. Two cases were osteogenic. One of these (fig. 23) recovered with X-ray therapy; the other (fig. 24) died after orbitotomy from wide intracranial extensions.

Figure 25 shows a case of retrobulbar sarcoma before and after the evisceration. Bone involvement of the roof of the orbit, necessitating extensive surgery, was the cause of the marked preoperative inflammatory reaction. This patient is still alive.

One patient responded immediately to X-ray therapy but left the city and, since then, all trace has been lost of him.

Figure 26 shows sarcoma in an infant who died of intracranial metastases in spite of therapy. Three cases of sarcoma were conjunctival, scleral, or subepithelial, all tumors being located in the region of the inner canthal angle.

It is quite proper to discuss, also, a small but by no means insignificant group of the rarer, or miscellaneous, tumors. These include, among others, two cases of hypernephroma, two cases of Ewing's tumor, three cases of mixed-cell tumor of the lacrimal gland, and one case of rhabdomyoma. In the miscellaneous group, these were the only tumors with mortality incidence.

Osteomas and lipomas were included in the original classification. Many rarer forms were not included for they did not appear in this period of time.

A single patient with rhabdomyoma, which started in the inferior rectus muscle, recovered from the rhabdomyoma (rhabdomyosarcoma?) but died subsequently from adenocarcinoma of the breast. This is one of two cases seen in this group of multiple malignancies.

Fig. 25 (Spaeth). Retrobulbar sarcoma before and after evisceration.

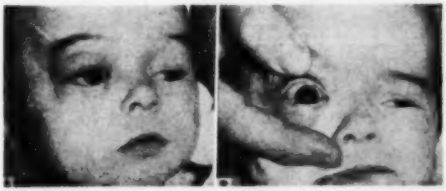


Fig. 26 (Spaeth). Retrobulbar sarcoma in an infant.

Two cases of Ewing's tumor were seen. Both terminated in death. One was that of a relatively young man in whom the first symptom was slowly developing exophthalmos.

Two cases of hypernephroma, or neuroblastoma, were seen, both terminating in death. The first of these two patients lived for about four months (fig. 27). The second one, a child, aged eight years, however, died within two months of the appearance of the orbital metastases. Evisceration, X-ray therapy, and nitrogen mustard were used.

There were three cases of mixed-cell tumor of the lacrimal gland. In two, the diagnosis was certain, being confirmed histologically and at autopsy. Diagnosis in the third case is still in question.

One of the two confirmed cases (fig. 28) was under observation for many years, the first surgery in this case having been done 18 years before the last surgery. This case, its course and progress, and a histologic study of mixed-cell tumors of the lacrimal gland, was presented before the College of Physicians of Philadelphia, Section of Ophthalmology, three years ago, by Dr. Edward I. Rubin.[5] There is much which is still to be written relative to this tumor.

The single osteoma and the single lipoma included in this group need no comment. Figure 29 shows an osteoma of the left orbit.

In this presentation, the carcinomas—including basal-cell types, squamous-cell carcinomas, or epidermoid carcinomas (nomenclature of Ward and Hendrick), and the intermediate (transitional) cell types of carcinomas which lie, clinically, between the basal-cell and squamous-cell types—are all classified in a single group. This would not be proper if clinical significance were to be considered because each type has differences as to position predilection, as to metastases, in mortality rates, and in the demands for treatment.

Fig. 27 (Spaeth). Neuroblastoma. Death shortly after these photographs were taken.

Fig. 28 (Spaeth). Mixed-cell tumor of the lacrimal gland. Evisceration 18 years after the first appearance, picture on extreme left. Death one year after the evisceration.

Fig. 29 (Spaeth). Osteoma of the left orbit.

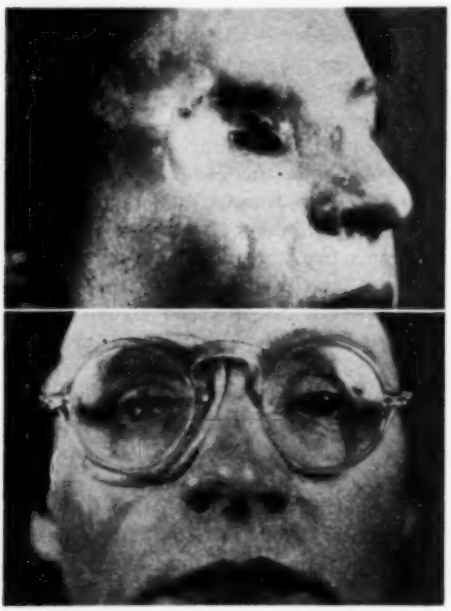


Fig. 30 (Spaeth). Recovery, after surgery for squamous-cell carcinoma of the lacrimal sac. Prosthesis being worn.

This large group of carcinomas is probably the most interesting of this entire series: It includes 60 cases. The epithelial-cell tumors comprised 37 percent of all malignancies.

Included in the cases of primary adenocarcinoma are involvements of the lid, the lacrimal gland, the conjunctiva, and the tarsus. The cases of metastatic adenocarcinoma included those with metastases from the maxillary sinus, from the breast, from the lung, from the prostate, from the ethmoid sinus, and from the maxillary gland.

There was one case of primary carcinoma of the orbit. There were five cases of primary carcinoma of the lacrimal sac with one death. Basal- and squamous-cell carcinomas of the lids were present in 35 cases.

The one patient with primary carcinoma of the orbit responded beautifully to radical surgery followed by X-ray therapy and is still alive after five years.

Three cases of carcinoma of the orbit which originated in the neighboring accessory sinuses are not included in this series. They were seen with various rhinologic services and were not considered as primary ophthalmologic situations.

There were five cases of squamous-cell carcinoma of the lacrimal sac. These cases all needed radical surgery. Figure 30 shows one such patient, wearing her prosthesis, four years after successful surgery. Figure 31 shows a similar case in which death, after three years, came from continued extension.

Adenocystic carcinomas, more commonly called adenocarcinomas, are grouped as a separate entity. It is rather interesting that, of the 18 such cases, nine were primary and nine were metastatic. These tumors are much more malignant than the basal-cell or squamous-cell types, produce extensive destruction of the soft tissues and the underlying bone, metastasize perhaps even more frequently than the squamous-cell types, and have a much higher mortality rate.

Fig. 31 (Spaeth). Squamous-cell carcinoma of the lacrimal sac, death followed extension.

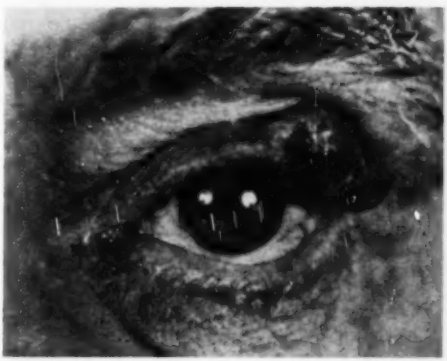


Fig. 32 (Spaeth). Adenocarcinoma, primary.

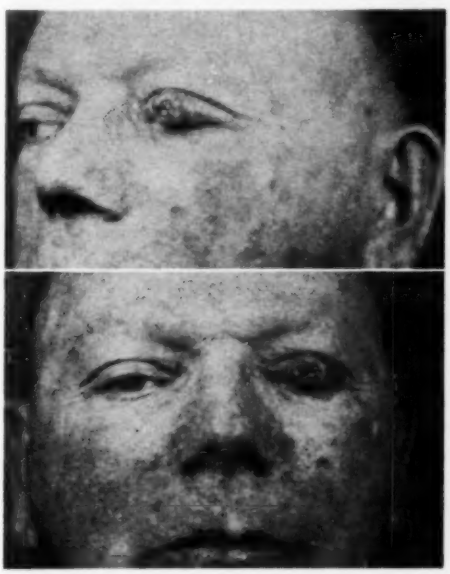


Fig. 33 (Spaeth). Adenocarcinoma, primary.

There have been five deaths among the nine cases of primary adenocarcinoma up to the present time. One patient with adenocarcinoma of the tarsus with extensive metastases to the cervical and submaxillary glands on the same side of the head (fig. 32) is still alive following extensive surgery and massive X-ray therapy. It is difficult to believe that she has been permanently cured, although she is now completing her second full postoperative year.

One case of adenocarcinoma of the tarsus (fig. 33) was that of a roentgenologist, who had further extensive surgery over a period of two years. The patient died following intracranial extension after the subsequent removal of a major portion of the nose, the upper lip, and the left malar bone.

There was one death in two cases of adenocarcinoma of the lacrimal gland. In one case of adenocarcinoma at the limbus, death resulted from the extension of the malignancy.

One patient, the brother of a Philadelphia physician, at the time of his death had three intraocular metastases in his left eye. His entire body, at autopsy, was studded with many miliary metastases. The generalized carcinomatosis was thought to have arisen from a group of glands found, at postmortem examination, behind the stomach.

There were nine cases of metastatic adenocarcinoma. Of these, five patients are known to have died and one, who refused surgery, disappeared. Only three patients of these nine recovered to live a minimum, so far, of four years.

One case, metastatic from the breast, was treated successfully with a radon seed; there was a complete recovery from the ocular malignancy. The patient died, however, a year later, with intracranial metastases.

One additional case, seen in consultation, is not included herein, since it was not treated at any time on our service.

In one case resulting in death, an intraocular metastasis from the lung, the history

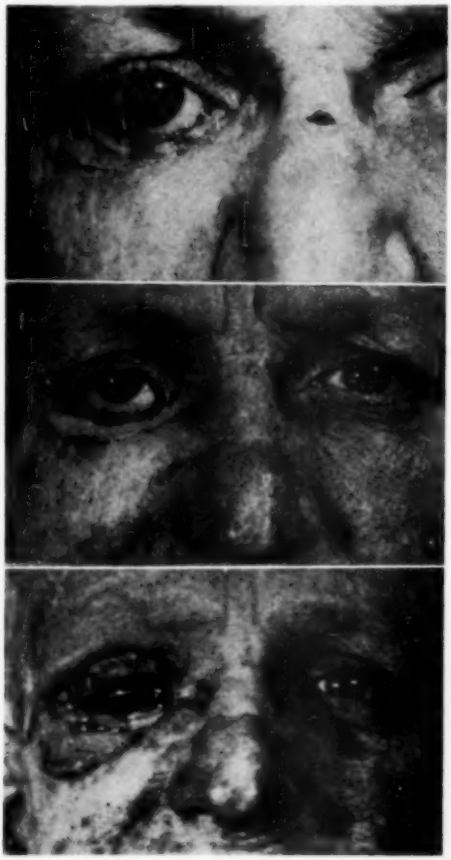


Fig. 34 (Spaeth). Basal-cell carcinoma with recurrence and reoperation, and with a recovery (now for two years). Initial malignancy occurred in the scars remaining from earlier lupus erythematosis.

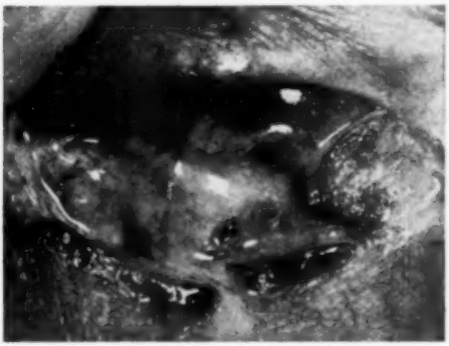


Fig. 35 (Spaeth). Squamous-cell carcinoma.

was tragic. I feel that the case was very poorly handled by the first ophthalmologist who saw it.

The patient reported to that ophthalmologist with a so-called retinal detachment. The only further examination made in this case, apparently, was a fundus examination. Advice was given to the patient that surgery should not be done, and, she was told further, "not to permit anyone to operate her at any time because it would be useless."

Several months later, the patient moved to Philadelphia and was then seen at the Graduate Hospital. Transillumination of the eye at that time, during routine examination, showed a solid retinal tumor. Routine X-ray examination of the lungs—a procedure which, with a blood serology investigation, must be done in every case which shows a defect in ocular transillumination—revealed bronchogenic adenocarcinoma.

An exploratory chest operation was done but the case was no longer operable. At that time, the operating surgeons believed that earlier diagnosis and either surgery or X-ray therapy, or both, might have been of value.

There were 35 cases of basal-cell and squamous-cell carcinomas. Four of these had recurrences. There were six deaths.

Figure 34 illustrates a basal-cell carcinoma with recurrence, reoperation, and recovery. Figure 35 is of squamous-cell carcinoma.

Figure 36 is basal-cell carcinoma of the caruncle. Figure 37 is basal-cell carcinoma of the lid margin, indolent, and without extension. Figure 38 shows a remarkable extension seen only by traction to uncover the extent of the malignant ulceration.

Figure 39 is basal-cell carcinoma involving the lid margin and the conjunctival surface. Figure 40 is one of primary mucus mem-

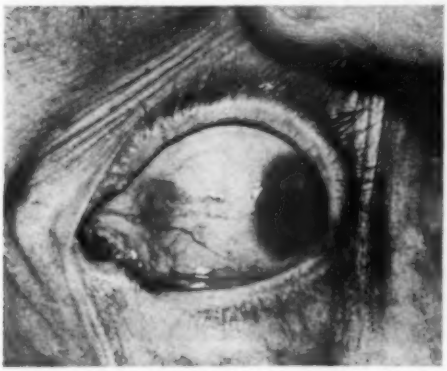


Fig. 36 (Spaeth). Basal-cell carcinoma of the caruncle, indolent for months.

Fig. 37 (Spaeth). Basal-cell carcinoma of the lid margin.

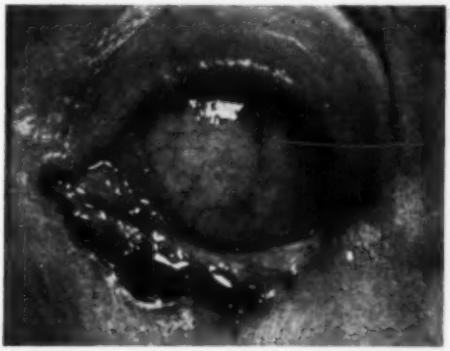


Fig. 38 (Spaeth). Basal-cell carcinoma of the lid margin.

Fig. 39 (Spaeth). Basal-cell carcinoma involving the lid margin and the conjunctival surface.

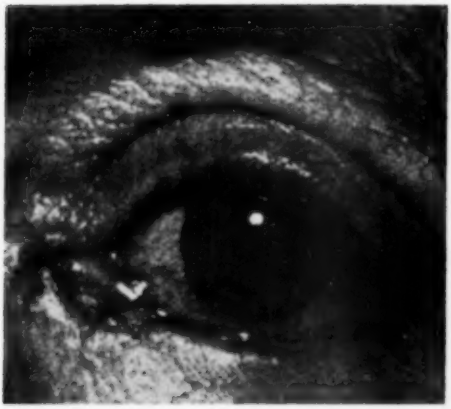
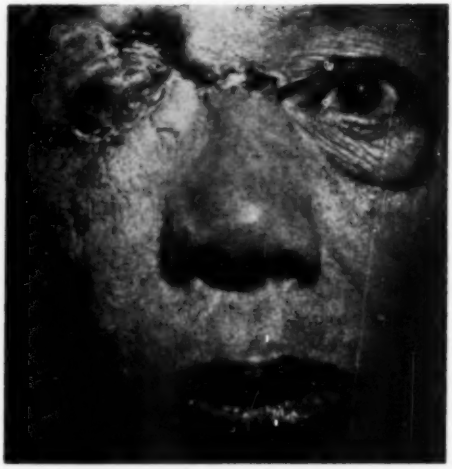
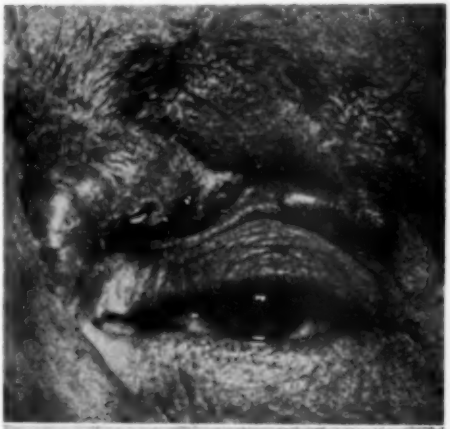


Fig. 40 (Spaeth). Primary mucus membrane involvement with secondary lid-margin extension.





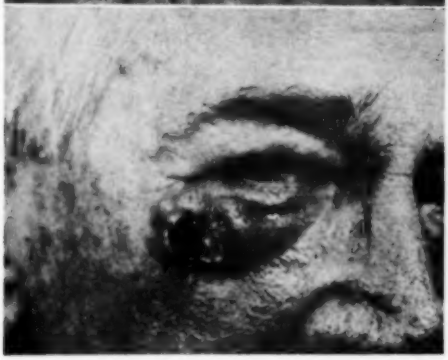


Fig. 41 (Spaeth). Scirrhous or intermediate type carcinomas of the lids.

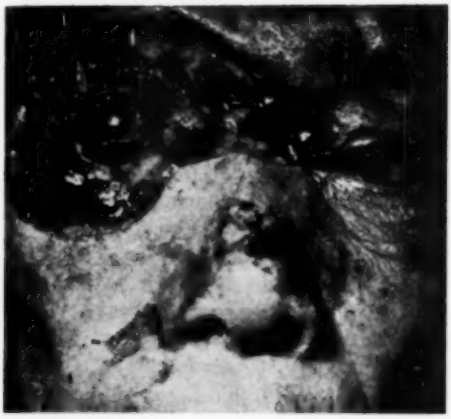


Fig. 42 (Spaeth). Carcinoma appearing in a skin graft used for earlier plastic correction.

brane involvement with secondary lid-margin extension.

Figure 41 shows two cases of scirrhous- or intermediate-cell carcinoma of the lid. One patient had had an earlier ovarian malignancy, with an apparently successful recovery from the oophorectomy.

Two other cases in this group are sufficiently interesting to be given in more detail. In one of these (fig. 42), presented originally in New England,[6] a malignancy developed in a skin graft used originally for the plastic correction of cicatrices from a third-degree burn. In the other case, one of squamous-cell carcinoma (fig. 43), I have operated on the patient repeatedly over a period of years. Her latest surgery, done approximately two years ago, included rather extensive removal of a portion of the malar bone. The entire orbit has been removed and with it the medial wall of the orbit, and the nasal cavity is easily viewed through the lateral wall and floor of the orbital cavity.

It is impossible to say that this patient *will* not have a further recurrence in the future. At the present time, however, the patient, in early adult life, is without any evidence of a continued advance in the carcinomatosis.

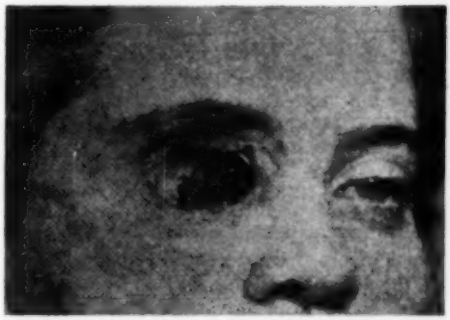


Fig. 43 (Spaeth). Carcinoma with extensive involvement of the bony orbit.

Conclusions

This series of cases, as presented and as illustrated, is shown largely for macroscopic diagnosis. It follows logically the earlier presentation on incidence.[1] A third presentation, to cover, in general, the treatment of the ocular tumors, is planned for the near future.

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Ophthalmic Miniature

. . . the tonometer may be utilized for the accurate measurement, not only of the intra-ocular pressure, but also of the index of ocular drainage.

M. J. Schoenberg, M.D.

Archives of Ophthalmology, **42**:117, 1913.

ANNULAR MALIGNANT MELANOMA OF THE IRIS AND CILIARY BODY*

Report of a case and summary of the literature

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Annular malignant melanoma is a tumor which grows circumferentially about the axis of the eye in the substance of the iris and ciliary body, with but little tendency toward the formation of tumor masses, and with limited invasion of the choroid. It is related to the "flat sarcoma" of the choroid, described by Fuchs,[1] in 1882, and perhaps to cancerous melanosis of the skin, both of which show the same quality of diffuse invasion of normal structure without the formation of masses.

Some malignant melanomas of the iris assume an annular form when their cells become loose in the aqueous and circulate into the filtration angle. The earliest case of annular malignant tumor of the eye on record, that of Solomon,[2] in 1882, was of this type.

In Solomon's case the primary lesion was not diffusely infiltrative, but an elevated mass, growing forward from the iris. However, he states, "The angle of the chamber is infiltrated throughout the whole of the circle by a mass of cells which have no direct continuity with the primary growth, but have evidently been brought there by the current of the aqueous humour."

Reese[3] asks that the distinction always be made between the type which is a ring by infiltration and the type which is a ring by dissemination.

Incidence

Annular malignant melanoma is distinctly an unusual condition. Dejean[4] refers to it as a "clinical curiosity." Wolff,[5] in his book, *Pathology of the Eye*, says merely that this type of growth is related to flat sarcoma of the choroid, and that it is "very rare."

Richardson[6] states that the descriptive literature dealing with tumors of the anterior uvea is often not clear enough to permit the reader to tell whether the circumscribed or diffuse type is being described, but says, "The diffuse tumor appears to be extremely rare." Only two authors have reported more than one case: Meyerhof,[7] in 1902, who reported three cases, and Richardson,[6] 45 years later, who reported two.

Murray,[11] who in 1927, gave the most recent complete tabulation of annular tumors, lists seven cases of annular tumor of the iris and 13 of the ciliary body. He adds one case of his own, which he calls an iris tumor, a total of 21 cases.

Richardson,[6] writing on "Diffuse malignant melanoma of the iris" in 1947, accepts only 14 cases of that type of iris tumor: six gathered by Li[8] in 1923, five additional gathered by Doherty[9] in 1939, one case of Martin-Jones,[10] and his own two cases.

One cannot avoid the impression, however, that, in these classifications, the classifers are depending on the titles given by the various authors to their individual papers, and that a tabulation on this basis is misleading. For instance, one report, that of Szymanski,[12] is entitled "Melanosarcome annulaire de l'iris," and is listed by all the just-mentioned authors under the heading of iris tumors. But Szymanski's illustrations and text show that the tumor he reports is just as much a tumor of the ciliary body as of the iris; it is a large mass, protruding from the ciliary body toward the axis of the eye. The author is certainly entitled to an opinion as to the primary site of the tumor, but it would be difficult to

* From the Graduate Hospital of the University of Pennsylvania, Service of Dr. E. B. Spaeth. Presented before the Philadelphia College of Physicians, Section on Ophthalmology, December, 1951.

put this case into the category of iris tumors to the exclusion of ciliary body tumors.

Some of the cases listed with annular iris cases seem almost surely to be primarily iris tumors, though in practically every case the ciliary body is invaded to some extent. Similarly, a few of the cases enumerated as annular ciliary body tumors can be reasonably assumed to be primarily ciliary body tumors, but all of them had invaded the iris. In a considerable number of cases, however, the tumor had invaded both the iris and the ciliary body to such an extent that it is difficult, or impossible, to determine the primary site of the growth.

Classification

A careful attempt to classify all the reported cases of annular malignant melanoma as either iris or ciliary body growths, therefore, would leave an appreciable percentage of unclassifiable cases. The iris and ciliary body are so closely related, and this type of growth shows such a strong tendency toward diffusion from one into the other, and there are so few of these tumors to classify, that I suggest we simply classify all of them as annular malignant melanomas of the iris and ciliary body.

Even though an author is convinced that a particular case is primarily one or the other, he can use the term with a clear conscience, since both structures are almost certain to be involved. The report should make clear the author's opinion as to the site of origin and whether the annularity is the result of dissemination through the aqueous around the filtration angle, or the result of diffuse growth through the annularly disposed iris and ciliary body.

In this connection Truc and Dejean[13] use the term "sarcome annulaire iridociliare," and Böje[14] "ringsarcoma iridis et corporis ciliaris" for their cases, both of which were tumors involving large amounts of both ciliary body and iris. These terms would be satisfactory were it not that the word "sarcoma" is open to criticism.

Cases in literature

If we may tabulate annular growths of the iris and ciliary body together, there are 31 unquestionable cases in medical literature. There are: 20 of the 21 cases gathered by Murray[11] in 1927 (Ref. 2, 7, 8, 11, 15-28); six added by Doherty[9] in 1939 (Ref. 12-14, 30, 31); one of Martin-Jones[10] in 1946; two of Richardson[6] in 1947; one of Nicolas[32] in 1947; Case 4 of Mary Knight's series.[26] My case makes the total 32 cases.

I have not included three cases which have been accepted by some writers on the subject. In the case reported by Ischreyt[29] the largest part of the tumor was extraocular. The tumor described by Kamocki[33] seems to be basically a flat sarcoma involving the ciliary body. However, a considerable amount of choroid was involved and, in one place, a large tumor mass was growing out of the choroid.

Kominsky's report in Russian is not available to me;* the German abstract[34] is too abbreviated to permit accurate evaluation. The case is described as a melanosarcoma of the ciliary body. Clinically, the tumor was a poorly outlined black spot on the iris. The abstract states:

"Microscopic examination showed a tumor measuring 11 by 4 by 4 mm. which had grown at the expense of the anterior portion of the ciliary body. It consists of round and spindle-shaped, richly pigmented cells which fill the lower portion of the anterior chamber and invade the iris and lens. The eroded lens is infiltrated with pigment granules." The reference given by Dejean, who accepts this case, is the German abstract.

Etiology

Several explanations are available for the ring shape of the annular malignant mela-

* Volume 5, p. 69, 1926 of *Russkij oftalmologičeskij žurnal* is not held by the library of the College of Physicians of Philadelphia. The *Union List of Serials* shows only two other libraries in this country carrying this title, the Welch Library in Baltimore and the Library of Congress, and neither is listed as having this number.

noma, but the question of why some tumors of the iris and ciliary body form rings, and some do not, remains unanswered. Nearly everyone who has written on the subject describes the vascular circles of the iris which may furnish both ready nutrition for the tumor and a potential space for its spread.

The older authors thought the tumors were of endothelial nature, with a natural tendency to spread across the surfaces. Pindikowski[15] went to great pains to show in his drawings the tumor cells growing in a layer across the anterior lens surface, about the iris, and across the cornea. Parsons[35] says, "The key to this will, I think, be found in their flatness and in their endothelial origin."

Dejean[4] says, "It is possible that ocular tension has an influence on the flat form of certain uveal sarcomas and that it is not unconcerned with annular forms." He believes that the ciliary muscle and the pigment layer of the iris form important restraints on tumor expansion, and refers to the ciliary muscle as the "ultimum moriens" of sarcomatous invasion. This factor must be of considerable importance, since in all except the most advanced cases, where description is adequate, the pigment layer of the iris and the ciliary muscle seem to form the inner boundaries of the tumors.

Diagnosis and Prognosis

The diagnosis of these tumors is often difficult. Most of the reported cases came to the doctor either because of a visible pigmentation of the iris, or because of the symptoms associated with raised intraocular pressure. When iris involvement is minimal, as in my case, and the intraocular pressure is late to rise, early diagnosis is almost impossible.

Retinal detachment, which is almost a regular accompaniment of malignant melanoma of the choroid, is found in only a small percentage of these cases. Astigmatism, iridodialysis, subluxation of the lens, and cataract have accompanied annular tumors. Because of their tendency to grow through the root of the iris, it is possible that the more frequent use of the gonioscope in cases of glaucoma will uncover some cases.

No information is available as to whether the prognosis of this type of tumor is appreciably different from that of other uveal malignant melanomas. The histologic structure of the reported tumors does not seem to be specific, and does not differ appreciably from that of malignant melanomas in other parts of the uveal tract.

Case report

The patient, a 49-year-old white man (hospital history number 201905), was seen first on November 9, 1950, with the complaint of blurred vision in the right eye of about three weeks' duration. He stated that in September, five or six weeks before being seen, he had struck the right side of his head against a car door with enough force to break the edge of his glasses. There was temporary swelling of the soft tissues at the point of impact, but no visual symptom at the time.

Two weeks later there developed redness, swelling, and a feeling of irritation of the lids on this side. This was diagnosed as poison-ivy poisoning, and treated with cold compresses. The swelling subsided rapidly but when the swelling went down, the patient noticed, for the first time, impairment of vision in the right eye.

In the office, vision with best correction was: R.E., 6/12—1; L.E., 6/5+. Examination showed the left eye to be normal.

In the right eye, there was no ptosis or exophthalmos. The conjunctiva was slightly injected. There was atrophy of the iris and the anterior chamber was a little shallow. A slight amount of iris pigment was present on the anterior surface of the lens, but there were no precipitates on the posterior surface of the cornea, and there was no relucency of the slitlamp beam in the anterior chamber. The reaction of the right pupil to light was thought to be less active than that of the left.

Tension was: R.E., 12 mm. Hg (Schiøtz); L.E., 18 mm. Hg.

Fundus examination showed a bullous separation involving most of the inferior and temporal retina. A retinal disinsertion was described in the 9-o'clock meridian. Field examination showed loss of most of the upper and nasal fields. Transillumination was done in the office and repeated in the hospital under anesthesia, and no area of impaired transillumination could be seen. On November 24, 1950, transscleral diathermy was done temporally in the region of the disinsertion.

Vision in the right eye after the operation was 6/22 and remained at that level until the patient's last office visit before the second hospital admission. On his first visit to the office after the operation there was ". . . some walled-off detachment in

the periphery." This receded. Each of the six times he was seen in the next six months, the retina was found to be flat, with no evidence of detachment. On July 6, 1951, he returned to work.

On September 7, 1951, he reported to the office and stated that he had had pain above the right eye for the past three days with spontaneous, abrupt decrease in vision. There had been no injury preceding this drop in vision. Examination showed a retinal separation involving the entire nasal, temporal, and inferior portions of the retina. Vision was 1/60. He was readmitted to the hospital. After he was put to bed, the retina flattened a little and there could be seen, in the extreme nasal periphery, a dark-brown, solid looking mass.

On October 2, 1951, the eye was enucleated.

Pathologic examination showed a malignant melanoma of the ciliary body, encircling the eye in the form of a ring; the largest irregularity of the contour was a lumpy swelling in the nasal portion, probably the part which had been seen prior to enucleation.

The tumor was limited almost entirely to the ciliary body with but little invasion of the choroid or iris. Anteriorly the compressed ciliary muscle was invaded to some extent but not broken through. The major vascular circle (which is anterior to the ciliary muscle) was free of invasion either within the lumen or in the perivascular tissue.

The canal of Schlemm was patent in all sections and there were no tumor cells demonstrable in it or in the filtration angle (fig. 1).

Histologically the tissue was not uniform. Part of the tissue was made up of large polygonal cells having large, round nuclei and distinct nucleoli. These cells tended to be closely packed with little or no tendency to form whorls or fascicules.

About an equal proportion of the tissue was composed of smaller, elongated cells, with oval nuclei, and distinct nucleoli. These cells showed a definite tendency to form columns with the long axis of the cells at right angles to that of the column.

There was a moderate amount of pigmentation, which was, perhaps, more prominent in the areas where the latter cells predominated. This tumor would be classified as of mixed fascicular and epithelioid type.

On the basis of argyrophil-fiber content, the tumor falls in Callender's group 2. There was a fine network of fibers around nearly all the individual cells, but there were a few areas where none could be seen.

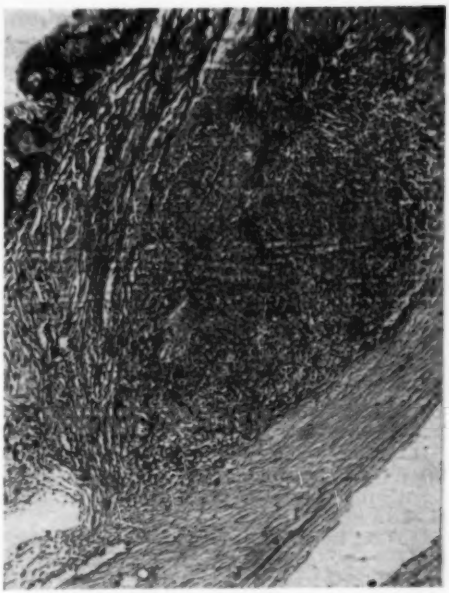

Fig. 1 (Rockwell). The tumor, on the right, has not penetrated the ciliary muscle. The filtration angle, the vascular circle, and the canal of Schlemm are not involved.

Comment

The freedom from involvement of the filtration angle, the circulus vasculosus major, and the canal of Schlemm show that the annularity in this case was not the result of invasion of these structures.

The histologic picture supports Dejean's description of the ciliary muscle as the ultimum moriens of invasion which would remove the above structures from consideration, since they are all anterior to the ciliary muscle. This case, though advanced, shows remarkably little tendency to break into the iris, and is undoubtedly primarily an annular tumor of the ciliary body.

Summary

The 32nd case of annular malignant melanoma of the iris and ciliary body has been reported. There was a retinal separation in this case which had all the appearance of a serous separation, and which responded temporarily to treatment with transcleral diathermy.

Although this particular case was clearly one of a tumor, primarily of the ciliary body with very little involvement of the iris, it is suggested that all tumors of this general type be classified as annular malignant melanoma of the iris and ciliary body.

The annularity could not be accounted for on the basis of involvement of the circulus vasculosus major, the filtration angle, or the canal of Schlemm.

This tumor was of the mixed type and did not differ, histologically, from other tumors, of mixed type but not of annular distribution.

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TOPICAL THERAPY IN INCLUSION CONJUNCTIVITIS*

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Introduction

The virus of inclusion conjunctivitis has been reported by various workers to be susceptible to the sulfonamides (Thygeson,[1] Thygeson and Stone[2]), to aureomycin (Braley and Sanders[3]), and to chloramphenicol (Leopold[4]). At the time of this writing, there is little evidence of its susceptibility to terramycin.

In view of the popularity and usefulness of sodium sulfacetimide† in the treatment of various eye infections, we have employed a 10-percent preparation of this drug in ointment base in a series of patients with inclusion conjunctivitis, and have compared its therapeutic effect with that of terramycin (0.1 percent) and aureomycin (0.1 percent) ointments. Insofar as it has been possible, the dosage and duration of treatment have been standardized so that the results with each of these three preparations could be compared.

Clinical material

1. Newborn infants

Since October, 1950, a study of eye infections in newborn infants on the public wards of the Toronto General Hospital has been in progress. All infants developing signs of ocular infection have been examined by us clinically, cultures were taken on blood-agar, and Peizer medium was inoculated for the gonococcus. In addition, scrapings taken from the conjunctival epithelium were placed on glass slides, fixed in methyl alcohol, and stained by the Giemsa method.

Sulmefrin ointment‡ was in use as a prophylactic agent during this phase of our study. Following the washing of the eyes with a sterile saline solution at birth, the sulmefrin ointment was applied by the intern to each conjunctival sac. As in the original Credé method employing a one-percent solution of silver nitrate, the sulmefrin was applied once only. This drug was not attended by signs of chemical irritation so commonly seen with silver nitrate.

Over a period of 11 months there were 1,703 births, and, of these, 97 infants developed conjunctivitis during the 10-day period in hospital. Inclusion bodies were found in conjunctival scrapings in seven of these infants. An analysis of the main etiologic agents found in this series appears in Table 1.

Treatment in this series was by topical application (four times daily) of either sulfacetimide, aureomycin, or terramycin ointments. Little difference could be seen between these three agents clinically. The response to therapy was similar with all three preparations with the conjunctival discharge

TABLE 1

Etiology of ophthalmia neonatorum
(Toronto 1950–51)

	Number of Cases	Percentage
Staphylococcus pyogenes	47	49
Diplococcus pneumoniae	11	11
Streptococcus viridans	11	11
Virus inclusion bodies	7	8
B. lactis aerogenes	4	4
Neisseria gonorrhoeae	3	3
B. antitratum	1	1
B. alkaligenes	1	1
B. coli	1	1
Negative (nonpathogenic staphylococci, C. xerosis, C. hoffmannii)	11	11
Total cases	97	100

* From the Department of Ophthalmology, University of Toronto.

† Sulfacetimide—Schering Corporation.

‡ Sulmefrin—E. R. Squibb & Sons.

TABLE 2

EFFECT OF TOPICAL THERAPY (OINTMENT BASE) IN INCLUSION CONJUNCTIVITIS

	Infants	Dosage	Cured	Recurred
Sulfacetimide	6	4×daily×14	6	0
Aureomycin	1	4×daily×14	1	0
Terramycin	2	4×daily×14	2	0

and inclusion bodies disappearing after 72 hours of therapy (table 2).

2. ADULTS

Using conjunctival scrapings taken from an infant with inclusion conjunctivitis, an eye of each of three adult volunteers was inoculated. The incubation periods in this group were 5, 7, and 16 days. Inclusion bodies were found in scrapings on the day of onset of symptoms in each case. The results of topical therapy in these three patients are seen in Table 3.

It will be seen from Table 3 that, in this group of adults, the effects of topical therapy were less dramatic than those seen in infants. Both symptoms and inclusion bodies persisted longer than they did in the infants.

Only one of these patients (G. A. T.) used aureomycin topically and, when his symptoms rapidly recurred after 14 days of therapy, all three patients elected to use terramycin ointment and continued its use for a minimum of 21 days. Although there was a fairly rapid relief of symptoms and disappearance of inclusion bodies with terramycin, there was a prompt recurrence of the disease following its discontinuance.

Sulfacetimide was then employed topically in each patient, and the response clinically did not appear any more rapid than with terramycin, but there were no recurrences after 14 days of therapy in two of the patients. In the third (G. A. T.) there was a recurrence, but a further course of sulfacetamide for 14 days was not followed by any further exacerbation.

In Table 4, the results of topical therapy in a group of 22 adult eyes are tabulated.

Two patients with inclusion conjunctivitis were referred to us following therapy with topical penicillin drops (1,000 u/cc.), and

TABLE 3

EFFECT OF THERAPY IN EXPERIMENTAL INCLUSION CONJUNCTIVITIS

Patient	Sex	Age	Incubation Period (days)	Therapy	Symptoms Ceased (days)	Inclusions Disappeared (days)	Cured	Recurred
E. J. H.	F	23	7	Terramycin ointment 21 days	4	4	No	Yes
				Sulfacetimide ointment 14 days	7	8	Yes	No
E. G. B.	M	22	16	Terramycin ointment 28 days	6	4	No	Yes
				Sulfacetimide ointment 14 days	7	9	Yes	No
G. A. T.	M	36	5	Aureomycin ointment 14 days	4	2	No	Yes
				Terramycin ointment 21 days	4	3	No	Yes
				Sulfacetimide ointment 14 days	5	4	No	Yes
				Sulfacetimide ointment 14 days	4	4	Yes	No

TABLE 4

EFFECT OF TOPICAL THERAPY IN INCLUSION CONJUNCTIVITIS IN ADULTS

Agent	No. of Eyes	Average Dosage (4×daily) (days)	Cured	Recurred
Sulfacetimide ointment	9	21	6	3
Aureomycin ointment 0.1%	4	28	0	4
Terramycin ointment 0.1%	6	21	3	3
Penicillin solution 1000 u/cc.	2	10	0	2
Sulfathiazole ointment 5%	1	21	1	0

inclusion bodies were found in scrapings in spite of this treatment. We were able to observe another patient treated by sulfathiazole ointment (five percent) by a referring physician. The response to therapy was excellent and there was no recurrence after 21 days of treatment.

All other patients were treated by us topically with either sulfacetimide, aureomycin, or terramycin, and we could see little difference in the effects of these three preparations insofar as suppression of symptoms was concerned.

Four eyes treated by aureomycin appeared clinically cured or markedly improved at the termination of the course of treatment, but there was a recurrence in each instance.

Terramycin ointment was successful in suppressing the clinical manifestation in all six eyes during the course of treatment but there were recurrences in three of the six eyes after therapy was discontinued. With sulfacetimide the response clinically was no more dramatic, but there were only three recurrent infections out of nine eyes treated, and these three were subsequently cured by a second course of treatment with this drug.

EFFECT OF CORTISONE

Five case histories illustrating the effect of cortisone in the treatment of inclusion conjunctivitis are given.

CASE 1

An infant (B. H.) developed a slight mucopurulent discharge in both eyes six days after birth. Conjunctival scrapings revealed the presence of inclusion bodies. On the following day the discharge was no longer evident so that treatment was withheld. Scrapings taken on six successive days failed to reveal any inclusion bodies and the conjunctivas appeared quite normal.

Cortisone ointment (two percent) was prescribed every two hours and continued for two weeks. On the fifth day of this treatment the conjunctival discharge reappeared and conjunctival scrapings henceforth revealed many inclusion bodies. Cortisone ointment was discontinued and the disease was terminated with sulfacetimide ointment.

CASE 2

A 33-year-old woman (J. H.) had had a follicular conjunctivitis in the right eye for four months prior to coming to the clinic. During that time her doctor had treated her with argyrol (four days), sulfacetimide ointment (10 percent, 35 days), aureomycin ointment (0.1 percent, seven days), penicillin drops (1,000 u/cc., 13 days).

Although she had improved under treatment there was still discomfort in the eye and there were a few follicles in the lower fornix and a slight enlargement of the preauricular lymph node. Repeated scrapings over a period of two weeks failed to reveal the presence of any inclusion bodies.

Cortisone ointment (two percent) was prescribed and the patient returned to the laboratory one week later. At this time there was more discomfort in the eye and inclusion bodies were found in the scrapings. The disease was finally terminated by sulfathiazole ointment (five percent) applied topically for 21 days. There has been no recurrence of symptoms after eight months.

CASE 3

A 29-year-old man (J. L.) had complained of some irritation in both eyes for about two years. For the past four months this had been quite severe and he had been treated by three different oculists during this period, all of whom had given him aureomycin drops or ointment. Although he was improved by this therapy he was still uncomfortable and more recently the vision in the left eye had become blurred.

Examination on admission to the clinic revealed broad bands of follicles in both lower fornices, enlarged preauricular nodes, and in the left cornea there were deep circumscribed infiltrates in the

substantia propria not unlike those seen in epidemic keratoconjunctivitis, but less sharply demarcated.

Repeated conjunctival scrapings over a period of two weeks failed to reveal inclusion bodies and, at the end of this time, cortisone ointment (two percent) was ordered every two hours. After one week of this therapy there was more conjunctival exudate present, the cortisone gave him no comfort, and at that time we were able to demonstrate inclusion bodies in scrapings taken from the conjunctivas of both eyes. The disease was finally terminated after a three-month course of 10-percent sulfactimide ointment.

CASE 4

A 26-year-old man (C. B.) had suffered from conjunctivitis for five years. He was referred to one of us (H. L. O.) in April, 1949, at which time a clinical diagnosis of inclusion conjunctivitis was made because of the broad bands of follicles in both lower fornices. The corneas were normal at that time. Repeated scrapings failed to reveal inclusion bodies.

He was not seen by us again till November, 1951. The follicles were now less prominent, but there were some adhesions in both lower fornices and there were stromal infiltrates in both corneas with extensive deep vascularization. For three weeks previously he had received cortisone ointment for the keratitis but the symptoms had been aggravated during this period.

Conjunctival scrapings now revealed many inclusion bodies. The disease was terminated by a three weeks' course of oral sulfadiazine combined with topical sulfacetimide ointment.

CASE 5

G. A. T., one of us, having recovered from an experimental inoculation with the virus of inclusion conjunctivitis following an extensive course of aureomycin, terramycin, and sulfacetimide ointments, was given a trial of cortisone ointment. No return of symptoms occurred and no inclusion bodies were found on repeated scrapings. It was concluded that he had been cured by his previous therapy.

DISCUSSION

Subsequent to our experiences with these patients, the commercial preparations of aureomycin ointment have been increased in strength from 0.1 percent to 1.0 percent. Similarly terramycin ointment is now available in 0.5-percent strength. It is possible that these more potent preparations will effect a cure in a higher percentage of adult patients with inclusion conjunctivitis.

It is of interest that in two of our patients with inclusion conjunctivitis, keratitis developed after the disease had been present for several years. Cortisone therapy did not appear to have any beneficial effect on this keratitis, and in four patients receiving this form of therapy it was possible to demonstrate inclusion bodies in conjunctival scrapings following treatment, whereas they had been absent prior to this.

SUMMARY AND CONCLUSIONS

1. Inclusion conjunctivitis in newborn infants was readily cured when treated topically for 14 days with either sodium sulfacetimide (10 percent), aureomycin (0.1 percent), or terramycin (0.1 percent) in ointment base.

2. In adults, inclusion conjunctivitis was readily suppressed clinically by these three agents employed topically. Exacerbation, however, occurred in all four eyes treated by aureomycin, in three out of six eyes treated by terramycin, and in three out of nine eyes treated by sulfacetimide. A second course of sulfacetimide successfully cured the infection in these three eyes.

3. In four patients with suspected inclusion conjunctivitis, inclusion bodies could not be found in repeated conjunctival scrapings. These were readily demonstrated following topical cortisone therapy.

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TRANSIENT ABOLITION OF THE PUPILLARY REACTION TO CONVERGENCE*

IN THE PRESENCE OF INTACT CONVERGENCE AND ACCOMMODATION AND NORMAL PUPILLARY REACTION TO ACCOMMODATION IN A CASE OF TUMOR OF THE PINEAL GLAND

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Jerusalem, Israel

In the literature dealing with disturbances of the pupillary reaction, no case was found in which the pupillary reaction to convergence was absent in the presence of normal convergence and accommodation and normal pupillary response to accommodation. It seemed therefore worthwhile to report such a case in order to draw attention to this condition.

CASE REPORT

History. D. M., a boy, 13 years of age, was sent to the Department of Neurosurgery (Dr. A. Beller, chief) on June 1, 1951, with a diagnosis of cerebral tumor. The family history revealed that his father had died at the age of 59 years from hypertensive heart disease; his mother had died at the age of 52 years from a lung ailment. One brother and a sister are alive and well. The boy was always well except that four years ago he suffered from an incontinence of urine which lasted for eight months.

Six months ago the patient began to suffer from severe headache, especially on the left side of his head. Five months ago he complained of diplopia and, at that time, his family noticed that the left eye was turned inward. The boy vomited several times a day. His head was always turned to the left side, there was a tendency to fall to the left, and his gait was uncoördinated. For the last two weeks, he was unable to move his head and during the last five days he was somnolent.

On physical examination the boy was found to be well orientated and in a satisfactory nutritional state. His blood pressure was 110/70 mm. Hg, and his pulse rate was 80 per minute. He could neither walk nor sit up, but lay in bed with his head straight. There was a limitation of the movements of the head and a marked opisthotonus. The skull was sensitive to percussion.

The patellar reflexes were absent, but the Achilles reflexes were present. Positive Babinski and Oppenheim signs were found on both sides. There was an ataxia of the upper and lower extremities, more marked on the right side. The Kernig sign was positive. Sensibility, superficial and deep, was intact. The abdominal and cremasteric reflexes were present.

Eye examination. The width of the lid fissure was equal on both sides. There was a paresis of both external recti with a slight convergent squint of the right eye. The upward gaze was paralyzed, the conjugate movement downward, and convergence were intact.

The pupils were dilated more in the left eye than in the right, the latter one being somewhat oval and eccentric (corectopia). The pupillary reflex to light was absent but there was a prompt near-reaction.

The fundus showed a papilledema of four to five diopters, accompanied by hemorrhages and exudates. The visual acuity was: R.E., 4/6; L.E., 4/5. The visual fields (confrontation test) appeared to be within normal limits.

Laboratory findings. The blood count showed slight anemia. The blood sedimentation rate was 1h35′ (Linzenmayer). The blood sugar was 86 mg. percent; urea, 32 mg. percent; Kahn and Wassermann reac-

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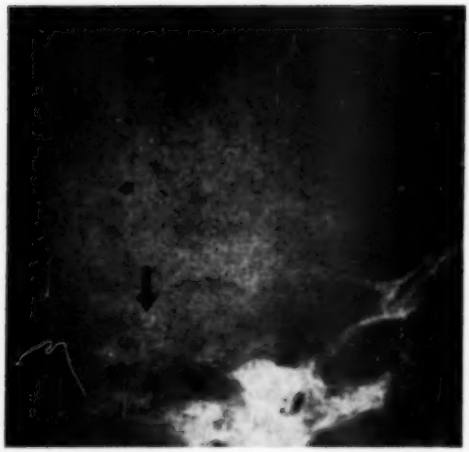

Fig. 1 (Kornblueth). X-ray film of the skull, showing a dense shadow in the region of the pineal gland (lateral position).

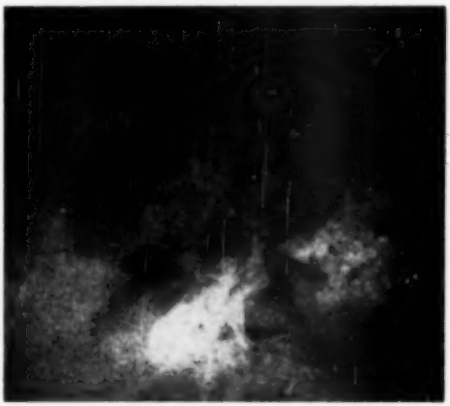

Fig. 2 (Kornblueth). Ventriculography, showing internal hydrocephalus with filling defect of the posterior part of the third ventricle (lateral position).

tions of the blood were negative. Urinalysis showed nothing abnormal.

X-ray studies of the skull revealed a definite shadow in the region of the pineal gland (fig. 1).

Five days after admission a pneumoventriculogram was performed by puncturing the left ventricle. It showed dilated ventricles with a filling defect in the posterior part of the third ventricle (fig. 2). The chemical analysis of the ventricular fluid revealed no abnormalities.

A diagnosis of tumor of the pineal gland (dermoid) was made, but the possibility of a posterior fossa tumor was considered. A cerebellar craniectomy was performed by Dr. Beller. No tumor of the posterior fossa was found.

Fluid was injected into the left lateral ventricle, but did not pass into the fourth ventricle. Because of closure of the aqueduct it was decided to use the Torkeldsen procedure, namely, connecting the left lateral ventricle with the cysterna cerebellomedullaris by a small rubber tube. The postoperative course was uneventful.

Examination of the eyes performed on June 18th (12 days after the operation) showed the following findings:

On looking straight, there was no devia-

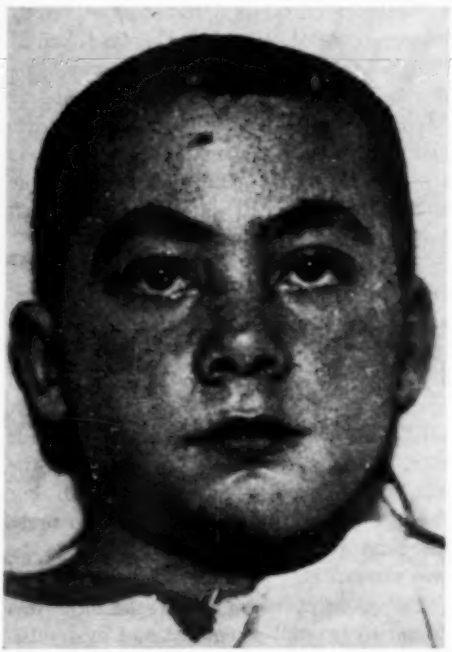

Fig. 3 (Kornblueth). No deviation of eyes on looking straight.

tion of the eyes (fig. 3). There was no limitation of lateral gaze in either direction (figs. 4 and 5). If the patient was told to look up, the eyes went into a convergence spasm instead (fig. 6).

The eyes, likewise, could not be elevated if the patient was ordered to look at an object lying above the horizontal plane (optically elicited movement). When, however, moving an object slowly upward and telling the patient to fix it, the eyes could be moved up for three mm. above the horizontal plane (following movement—fig. 7). There was some slight degree of diplopia.

The size and form of the pupils were unchanged as compared with the first examination. The pupils reacted very sluggishly to light, hardly at all to convergence (observed while in convergence spasm), and very promptly to accommodation. The amplitude of accommodation was about 10 diopters in both eyes. When forcibly closing the lids the

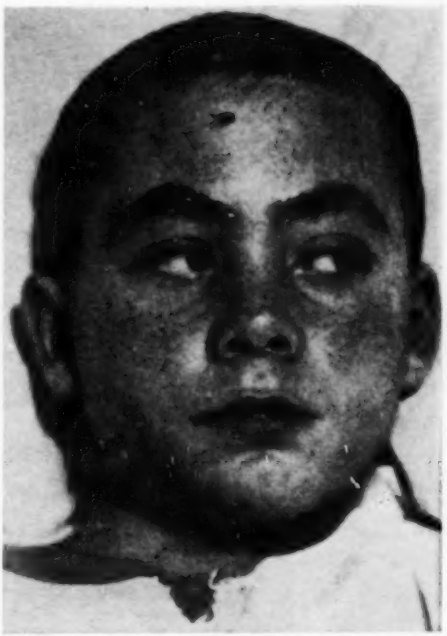

Fig. 5 (Kornblueth). No limitation of ocular movement on looking to the left.

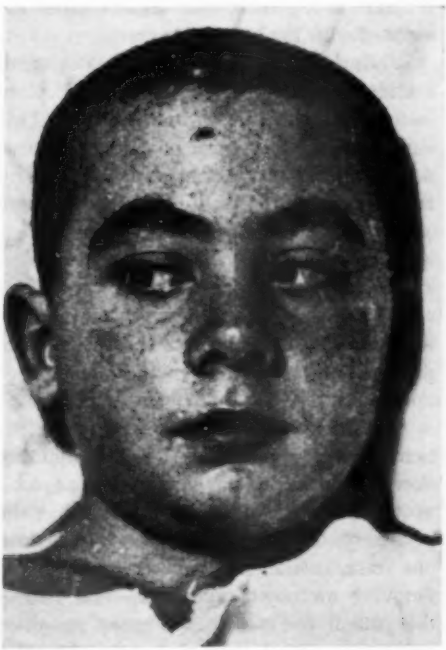

Fig. 4 (Kornblueth). No limitation of ocular movement on looking to the right.

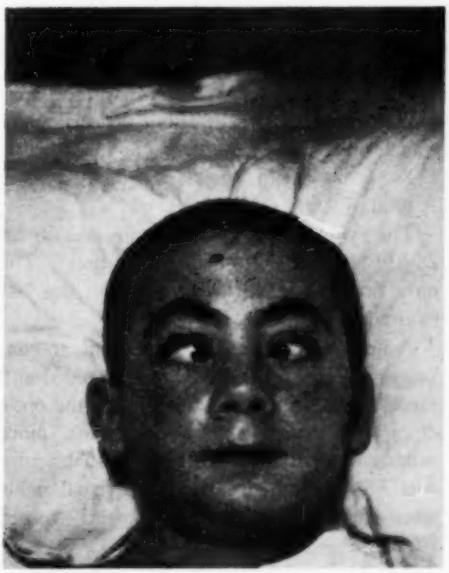

Fig. 6 (Kornblueth). On trying to look upward the eyes converge instead.

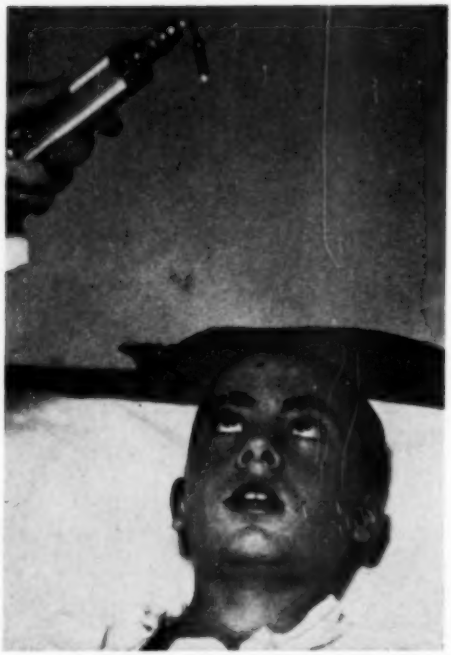

Fig. 7 (Kornblueth). Elevation of eyes above horizontal plane on following movement.

eyeballs moved up and out and the pupils contracted.

On ophthalmoscopic examination, papilledema on both sides of about three diopters was seen.

X-ray treatment was started on July 19th. A total of 9,600 r was given.

The eyes were examined again on August 28th (12 weeks after the operation). The only findings which differed from the last examination were:

A noticeable reaction of the pupils to convergence. The papilledema had subsided and there was only slight hyperemia of the optic discs with blurring of the margins, more pronounced on the right side. Visual acuity was 5/4 in both eyes and the visual fields were full to white (5/330) and to red (2/330).

The last examination of the eyes was performed on September 12th (14 weeks after the operation). This time the pupils showed a good response to convergence. All other findings remained unchanged.

At this time the vestibular compensatory reflex was tested and found to be positive (bending the head down briskly caused an elevation of the eyes above the horizontal plane). This test could not be performed before because of the impossibility of moving the patient's head.

The patient left the hospital greatly improved. The only neurologic deviations were absence of the knee jerks and a faint positive Babinski and Oppenheim sign on the right side.

Comment

This case presented most of the eye signs typical for a lesion involving the region of the superior colliculus: Pupillary disturbance, limitation of upward gaze, sixth-nerve palsy, and papilledema. A corectopia as observed in our patient was described by Wilson[1] in mesencephalic lesions often associated with Parinaud's syndrome.

When the patient was told to look upward, a strong convergence movement took place instead but the pupils did not contract. This tonic convergence spasm on intended elevation of the eyes was not infrequently seen by Bielschowsky[2] in paralysis of the elevators of the eye. According to Kestenbaum[3] it belongs to the group of comovements or synkinetic phenomena, meaning that "in paralysis of a muscle or a function, the innervation goes off to another muscle or muscle-group in a kind of overflowing of dammed-up impulses."

The schematic movement (telling the patient to look up), as well as the optically elicited movement (showing an object to look up to, the image of which is situated in the periphery of the retina), was affected in our case, while the following movement (moving an object slowly up and having the patient fix it with his gaze) remained intact.

Bielschowsky[4] calling the optically elicited

movement "attraction movement" assumed an occipital center for both the following and attraction movements. "If the pathway descending from the occipital center is injured but not fully interrupted, the patient may be unable to make an attraction movement of great extent, but he is able to make a small movement indeed by the excitation of the paracentral retinal points."[4]

The supranuclear nature of the lesion in our case could be concluded from the persistence of the following movement as well as the vestibular compensatory movement and Bell's phenomenon.

The vicinity of the pupillomotor fibers and the supranuclear tracts for vertical movements explain readily the disturbances of the pupillary reactions associated with anomalies of vertical movements.

The near reaction of the pupils is composed of two components: (1) Convergence reaction; (2) accommodation reaction.

The stimuli for the convergence reaction are the proprioceptive impulses arising from the contraction of the two internal recti, while the accommodation reaction is stimulated by perception of a blurred image of near objects.

Usually both reactions combine to give a constriction of the pupils. It is well known that each of the reactions may function independently without the other one.

With lenses or prisms, either accommodation or convergence can be eliminated, but the pupils will still constrict in association with the unaffected function. In certain cases of blindness, in spite of a nonexisting accommodation, a voluntary convergence will produce constriction of the pupils.

On the other hand, in the ocular type of progressive muscular atrophy, in which both internal recti are affected and no convergence is possible, the pupils will constrict on accommodation. It follows that two different pathways have to be assumed for the pupillary reactions, one for convergence and another for accommodation.

Leatheart[5] gives the following scheme for the pathways: The pupillary reaction to accommodation, the "blurred image reflex" travels from the retina → visual fibers of optic nerve and optic tract → lateral geniculate body → optic radiation → striate cortex → area 19 → cortical association pathway → internal capsule → nucleus of Perlia → parasympathetic fibers to ciliary muscle and constrictor iridis. These latter fibers do not pass through the ciliary ganglion.

The afferent limb of the pupillary convergence reflex travels from the two internal recti through the trunk of the oculomotor

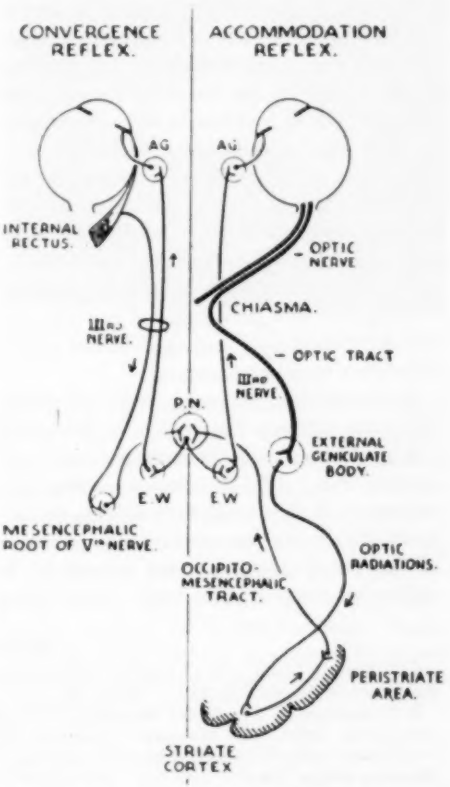

Fig. 8 (Kornblueth). The pathway of the near reflex showing the two components. (Reprinted with permission from Duke-Elder,[7] *Textbook of Ophthalmology*. London, Henry Kimpton, 1949, v. 4, p. 3794.)

nerve to the nucleus of Perlia. The efferent limb is common to the accommodation reflex. In a later paper Leatheart[6] drew a scheme for the pathway of the convergence reflex, but here the afferent limb passed from the internal recti along the ophthalmic branch of the trigeminal nerve and not along the oculomotor nerve.

According to Duke-Elder[7] (fig. 8), the pupillary convergence reflex "is activated by proprioceptive impulses of the two internal recti; the path of the afferent fibers is unknown; they may travel up the ophthalmic division of the fifth nerve but more probably ascend the third nerve to reach the mesencephalic root of the trigeminal, thence a relay is made to Perlia's nucleus, whence connection is made with Westphal-Edinger nucleus." "From the constrictor center the afferent path is common to the two reflexes (accommodation and convergence)."

A lesion in the midbrain affecting the afferent limbs of the convergence pathway between a mesencephalic root of the trigeminal and the nucleus of Perlia could theoretically cause an abolition of the pupillary reflex to convergence with persistence of convergence and accommodation, and undisturbed pupillary reflex to accommodation.

In my opinion, the reason that such a condition has not been described is twofold: (1) Cases showing this phenomenon are extremely rare; (2) in routine clinical examination of the pupillary reactions, the accommodation and the convergence reactions of the pupils are not tested separately. It might be that, if this were done, more cases of the kind herein described would be diagnosed.

In this case the favorable circumstances of dissociation of convergence and accommodation (convergence spasm in trying to look upward) allowed me to observe the pupillary reaction to convergence distinctly from that of accommodation.

Summary

A case of a tumor of the pineal gland is described which showed dilated pupils, corectopia, absence of pupillary light reflex, paralysis of upward gaze, convergence spasm, paralysis of the external recti, and papilledema.

The most remarkable finding was a temporary abolition of the pupillary reaction to convergence while convergence and accommodation, as well as the pupillary reaction to accommodation, remained intact.

A lesion affecting the afferent limbs of the pathway for the pupillary reaction to convergence between the mesencephalic root of the trigeminal and the nucleus of Perlia within the midbrain might possibly have caused this pupillary disturbance.

It is suggested that this condition has not been diagnosed heretofore because of its rare occurrence and the lack of testing separately the pupillary reaction to convergence and accommodation in routine clinical examinations.

Rothschild Hadassah University Hospital.

Acknowledgement

I wish to express my thanks to Dr. A. Beller for permitting me to examine and report this case.

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NOTES, CASES, INSTRUMENTS

CONTACT LENSES FOR GONIOSCOPY AND OPHTHALMOSCOPY

OTTO BARKAN, M.D.
San Francisco, California

CONTACT LENS FOR GONIOSCOPY

Gonioscopic contact lenses designed by Koeppe[1] in the form of an "A" lens and a more convex "C" lens suggested by Troncoso[2] have a diameter of 22 mm. As they are too large for the palpebral fissures of some individuals and for most children, I designed a plastic lens made of methyl-methacrylate similar to the Koeppe "C" lens.[3]

This lens is lighter in weight, provided with a short plastic handle, and is made in five diameters from 18 mm. to 22 mm., so that all palpebral apertures can be accommodated.

Since the plastic lens mars easily, a series of glass lenses of different diameters 16 mm., 18 mm., and 20 mm., have been designed. Being made of glass they possess optical advantages (fig. 1). They have an anterior radius curvature of 12 mm. and an inherent magnification of ×1.5.

A dimple at the apex has been retained but is smaller than in the original Koeppe lens. It facilitates holding the lens in position by the tip of the finger or by an applicator.

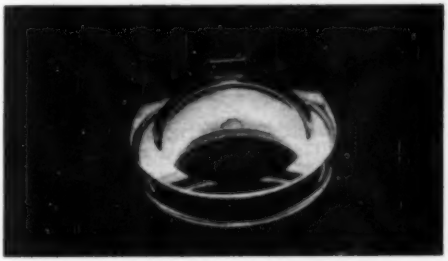

Fig. 1 (Otto Barkan). Contact lens for gonioscopy.

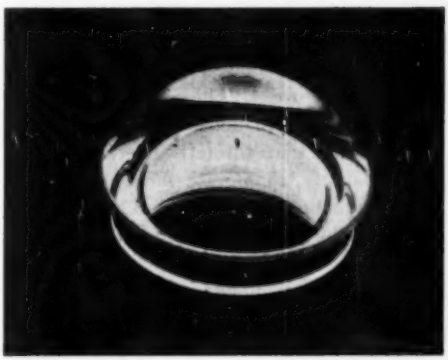

Fig. 2 (Otto Barkan). Contact lens for ophthalmoscopy.

CONTACT LENS FOR OPHTHALMOSCOPY

In many cases of congenital glaucoma although the cornea is clear to inspection, the optic disc and fundus appear blurred to direct ophthalmoscopic examination. If ophthalmoscopy is done through a gonioscopic contact glass, a sharply defined picture of disc and fundus is obtained. The explanation of this phenomenon appears to be that the blurred image is caused by irregular corneal astigmatism, the effect of which is eliminated by the contact glass. The glass can be used to serve the same purpose in adult eyes in which the image of the fundus is blurred by corneal scarring and astigmatism. This is the reverse of what occurs in adults with irregular astigmatism whose visual acuity is improved by the wearing of a contact glass. These ophthalmoscopic lenses are made in three sizes but without the dimple (fig. 2).

490 Post Street (2).

The lenses are manufactured by Parsons Optical Laboratories, 518 Powell Street, San Francisco.

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CORRECTION OF DIPLOPIA FOLLOWING THYROIDECTOMY

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New York

CASE REPORT

E. S., a white woman, aged 48 years, presented herself for treatment on May 13, 1947. Her chief complaints were double vision and increased protrusion of the right eye. She had had a subtotal thyroidectomy on October 5, 1946, to relieve toxic exophthalmic goiter. The patient's symptoms (other than her eye symptoms) had been completely relieved by the operation.

Examination showed the condition revealed in Figure 1. There was a moderate degree of exophthalmos, two mm. more in the right eye than the left. There was complete inability to elevate the right eye in either adduction or abduction. On attempted elevation the right upper lid retracted considerably.

There was a troublesome diplopia varying from zero degrees in the reading position to approximately 35 prism diopters in the position of elevation. The deviation was approximately the same in eyes up and right as in eyes up and left. There was no interference with motility of the left eye.

Fig. 1 (McClanahan). Appearance of patient before the muscle operations.

Fig. 2 (McClanahan). Appearance of patient three and one-half years after corrective surgery.

Vision was normal in each eye without glasses. The eyegrounds showed nothing remarkable.

The patient was presented at the New York Eye and Ear Infirmary clinic and opinions varied from the extremes of leaving the condition alone to the suggestion of operating on four muscles.

On June 1, 1948, it was decided to explore muscular attachments of the right eye under general anesthesia. Fortunately the right inferior rectus was selected first. The muscle was isolated and freed with blunt dissection with some difficulty. The tendon was then sectioned and the muscle recessed a distance of four mm. Nothing further was done at this time.

Several days after operation the right eye could be elevated partially and the field of double vision had greatly decreased. Appearance was greatly improved.

On July 20, 1948, the left inferior oblique was recessed eight mm. and at the same time a Wheeler canthoplasty was done on the lids of the right eye.

By August 17, 1948, there was single binocular vision for the primary position and for moderate ductions. The patient was able to return to work as a saleswoman.

On February 1, 1952, the patient reported to say that she had been promoted to buyer for a large department store. Vision was 20/20 in each eye without glasses. There was single binocular vision in the six cardinal directions of gaze. Small deviations could be screened in the extreme ductions. There were no complaints. The proptosis had decreased. The appearance of the eyes on February 1, 1952, was as in Figure 2.

The patient has not taken any medication since the operation. She has not returned to her doctor for determination of basal metabolic rate. There are no symptoms of hypo- or hyperthyroidism at present.

Conclusion

The deformity in this case was probably due entirely to the adhesions around the right inferior rectus. The recession of the left inferior oblique could probably have been omitted with an equally good result. What appeared to be a paresis of elevation in the right eye turned out to be due to adhesions around the direct antagonist. The value of exploration in such cases is emphasized.

63 East 78th Street (21).

INSERTION OF OCULAR PROSTHESES AT AUTOPSY*

Myer M. Medine, M.D., Carlton C. Phillips, M.D., and Hilda Bergen
New York

It has been possible at this hospital to obtain permission for removal of eyeballs at postmortem examination in an average of 16.9 percent of cases in 1949, 1950 and 1951. This has proved of particular value because in a large general hospital for chronic diseases it has offered the opportunity to study the macroscopic and histologic changes in the eyes of patients with a variety of constitutional diseases.

In contrast, eyes studied in specialized institutions are limited macroscopically and histologically to those conditions which necessitated their removal during life.

A further objective of postmortem enucleation is to obtain fresh corneal tissue suitable for use in keratoplasties.

Until 1949, the technique used at this hospital was that described by Gartner and Lubkin.† With this method, the artificial eyes were secured by means of double-armed sutures which were either attached to both ends of the prosthesis with Canada balsam or passed through two holes which had been drilled through the periphery of the artificial eye. The sutures were then passed through the inner and outer canthi and tied beneath the lids.

This technique definitely required the services of an individual who was familiar with the procedure and often proved to be difficult and time consuming. Therefore, in order to permit enucleation of the eyeball and restoration of the socket as expeditiously as possible the procedure was modified.

Technique

The first step is to select two artificial eyes which correspond to the subject's in size of pupil, color of iris, and scleral markings. A speculum is introduced to keep the lids separated and the cilia everted. The conjunctiva is divided as far from the limbus as possible, as is Tenon's capsule.

Each rectus and oblique muscle is isolated in turn on a squint hook and sectioned with strabismus scissors. With the eyeball dislocated forward by pressure on the speculum, the optic nerve is first stretched and then divided with enucleation scissors. It is obviously desirable to obtain as much of the extraocular muscles and optic nerve as is feasible. The lacrimal glands are then removed by dissection.

A slab of plaster-of-paris bandage (40 by 10 cm.) is immersed in cold water and compressed to a round wad of approximately three cm. in diameter. With the speculum still in place, the plaster-of-paris bandage is introduced into the orbit and the prosthesis is inserted over it. After the proper alignment of the artificial eye, the excess of plaster is wiped away with moist gauze and the speculum is removed. The lids are closed and a piece of gauze soaked in formalin (40 percent) is placed over them for five minutes to harden them.

In the past two years over 200 eyeballs have been removed and artificial eyes substituted in accordance with the technique described. There has been no adverse criticism from morticians and next-of-kin, from a cosmetic point of view.

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* From the Eye Laboratory, Dr. Samuel Gartner, attending ophthalmologist, Montefiore Hospital.

† Gartner, S., and Lubkin, V.: Eyes from autopsies. Am. J. Ophth., 27 :527, 1944.

Summary

1. A new method for insertion of ocular prostheses following autopsy enucleation is described.

2. The method consists in filling the orbital cavity with a plaster-of-paris bandage and mounting the prosthesis on it.

3. The simplicity of this procedure has made it possible for eyeballs to be removed quickly and easily at autopsy. This has resulted in a greater yield of material.

57 West 57th Street (19).

CONJUNCTIVAL TUBERCULOSIS TREATED WITH STREPTOMYCIN

Peter Sykowski, M.D.
Schenectady, New York

Prior to Woods's[1] treatise on the therapy of ocular tuberculosis with promizole and with streptomycin, a case[2] of conjunctival tuberculosis treated simultaneously with intramuscular and topical streptomycin was observed in 1948. The present report is that of another case of primary conjunctival tuberculosis treated with streptomycin administered topically in the form of drops.

Report of case

A. J., a 40-year-old white man, was seen during January, 1949, with the story that for approximately five months he had had a "sore on his right lower lid."

Examination of the right eye showed in the middle one third of the lower lid in the subtarsal region a conjunctival ulcer, measuring 3.0 by 5.0 mm., irregular in shape, with a gray base; the surrounding area was intensely hyperemic. The preauricular lymph gland was definitely enlarged but not tender. The anterior cervical glands were palpable. Tuberculosis was diagnosed after a biopsy section of the conjunctival ulcer showed the presence of tubercle bacilli.

Treatment was immediately instituted with 10,000 units cc. of streptomycin instilled into the cul-de-sac, three drops, every two hours.

The course was uneventful. In five days, the ulcer remained approximately unchanged; in 12 days, the base began to clear, and in 20 days the ulcer was completely healed, being replaced by a white cicatrix. When seen during June, 1949, and during December, 1949, the cicatrix was smaller in size, measuring about one mm. in diameter.

Discussion

Garcia[3] cured a case of hypertrophic, nodular, caseating, palpebral conjunctivitis with conjunctival-sac instillations and with subconjunctival injections of a solution of streptomycin containing 10,000 units/cc. The diagnosis of tuberculosis was established histologically.

Das Gupta and Usman[4] healed bilateral tuberculous ulcers of the bulbar conjunctiva, resistant to ordinary therapy, with streptomycin drops of high concentration.

The present case was treated with streptomycin drops administered topically, the cure being effected in 20 days.

Conclusions

A case of an ulcerative palpebral conjunctival tuberculosis, the diagnosis being established histologically, was successfully treated with local instillations of streptomycin drops, in the concentration of 10,000 units/cc.

1330 Union Street.

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STRABISMUS IN TWINS*

STANLEY MASTERS, M.D.
Brooklyn, New York

The prevalence of squinting twins, although not rare, is sufficiently uncommon to provoke lively interest among ophthalmologists and students of genetics. In view of this general concern and the presence of certain findings peculiar to these twins, I believe that this study is worthy of notation.

CASE REPORT

Full-term monozygotic twins with strabismus were first seen in the Eye Clinic of The Long Island College Hospital in December, 1950. In addition to their mirror imagery a single placenta was reported which would substantiate origin from a single ovum. Both children were delivered by breech extraction. Child A weighed 6 lb., 10 oz. at birth, and Child B weighed 6 lb., 2 oz. Child A was well and had an uneventful postnatal period. Child B was delivered with considerable difficulty, and suffered a fracture of the right humerus. The child was born cyanotic and resuscitation was required before the child was able to maintain himself. There were no convulsions at any time.

The mother had a four-plus Wassermann reaction prenatally, and was treated at the clinic for this. Both children had a positive cord Wassermann reaction, although Child B had a negative serology at a later date. No abnormal pathologic condition was noted in the placenta.

Following birth, both children developed normally and were walking at the age of one year. They were slightly hyperactive, anxious, and developed a mild stutter. The mother first noticed their squinting when they were five years of age, following recovery from measles.

Two years prior to attending our clinic they were refracted but did not wear their correction with any regularity. When they were presented at our clinic they were eight years of age with a history of squint for three years.

Child A was a left-handed, well-developed, asthenic boy presenting a left concomitant esotropia of 60 prism diopters for near and distance with a near point of convergence of 125 mm. The measurements for distance were greatly impeded by poor fixation but, at best attempts, were the same as the near measurements.

Vision was: O.D., 6/15; O.S., 6/60. Refraction showed: O.D., +3.0D. sph. ⌒ +1.75D. cyl. ax. 105°, corrected to 6/9; OS., +4.0D. sph. ⌒ +2.5D. cyl. ax. 90°, corrected to 6/60.

The child evidenced some spastic element with accommodative effort and exhibited weakness of the left external rectus behind cover.

Child B was a righ-handed, well-developed, asthenic child, more anxious than his brother, and presented a right concomitant esotropia of 78 prism diopters for near and 62 prism diopters for distance with a near point of convergence of 93 mm.

Vision was: O.D., 6/30; O.S., 6/15. Refraction showed: O.D., +8.0D. sph., corrected to 6/15; O.S., +3.0D. sph. ⌒ +2.0D. cyl. ax. 90°, corrected to 6/9.

A weakness of the right external rectus was demonstrated behind cover.

There is a report of a squint on the paternal side; however, corroboration was not obtainable.

DISCUSSION

A review of the literature,[1-7] which included 19 pairs of twins, revealed certain salient features. Of these the characteristics of the squint and the studies on refraction were most interesting.

Both children reported in this case exhibited a squint which was essentially similar. This would generally be anticipated in a pair of monozygotic twins. The literature[1, 5-6] tends to substantiate this observation but several discrepancies have been reported. In

* From Long Island College Hospital.

seven separate studies comprising 19 pairs of squinting twins, 13 exhibited strabismus in both twins. Of these, the angle of deviation was similar in both twins and in the same direction of gaze. Of the six remaining, only one twin in each pair presented evidence of squint.

Wilson[5] observed, during a study of the refraction of twins, a discrepancy greater than one diopter in 41.5 percent as compared to 70 percent in siblings of different ages. This generally agreed with the findings of Law.[6] In several instances[2-4] the refraction was remarkably similar.

The children presented in this case study demonstrated a considerable difference in their refractive errors. A glance at Evans'[8] modification of Brown's refraction curve would indicate that the squint which developed at the age of five years, coincided with the time at which hyperopia was approaching maximum (this is 3.25 diopters of hyperopia at about seven and one-half years of age). At the age of eight years, the hyperopia had probably passed its peak, and was in the process of diminishing.

Refraction of the first child at that time revealed only a small departure from the average. Child B, however, revealed a definitely pathologic refractive error of the right eye.

Conclusions

1. A pair of monozygotic twins, each presenting a squint, was presented.

2. The presence of a squint in one twin is generally accompanied by strabismus in the other.

3. The refraction errors in pairs of twins can vary from striking congruity to unusual dissimilarity.

4. The refraction error may vary with the age of the individual and as such there may exist a direct relation between refraction, strabismus, and the age of the patient.

Long Island College Hospital (2).

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Ophthalmic Miniature

The great and sudden variability of climate, and the peculiarily moist state of the Irish atmosphere, appears to promote the rapid growth of that condition of the eyelids denominated as "granulation," and also to produce those frequent relapses to which such patients are liable.

W. R. Wilde,
Medical Times, London, 1862.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

January 7, 1952

DR. ADOLPH POSNER, *president*

PROBLEMS IN OPHTHALMOSCOPY

During the instruction period, DR. HOWARD J. AGATSTON presented a paper on this subject.

OPHTHALMOSCOPIC FINDINGS IN KIMMELSTIEL-WILSON SYNDROME

DR. MARTIN COHEN said that intercapillary glomerulosclerosis is a renal degenerative lesion prevalent in diabetes mellitus. The condition was first described by Kimmelstiel and Wilson in 1936.

The diagnosis of intercapillary glomerulosclerosis can be verified only by a postmortem renal examination, but a long-standing case of mild diabetes with retinopathy and renal dysfunction is strong evidence of a Kimmelstiel-Wilson lesion. It has been stated that intercapillary glomerulosclerosis occurs in nondiabetics, but this contention in most of the reported cases has not been confirmed by Allen's investigations. Retinal capillary microaneurysms have been observed and recognized in the early stages of diabetes mellitus, but are considered by some authors as nonspecific for diabetes.

The prognosis of intercapillary glomerulosclerosis, if clinically established, depends on the severity of the associated lesions and the effect of recognized treatment for diabetes mellitus. Continued investigation of this subject is important, in order to evaluate the varied opinions which have appeared recently in the literature.

Discussion. Dr. Lyons asked Dr. Cohen whether there was anything specific about the fundus findings in this condition. To which Dr. Cohen replied that this was a mixed case of diabetic retinopathy with complications of hypertensive retinopathy.

MANAGEMENT OF RETINAL SEPARATION

DR. P. ROBB MCDONALD (Philadelphia) said that he believes there is a very definite increase in the number of retinal detachments now being seen in ophthalmic institutions. This may be due to an actual increase in the incidence of the disease or more cases are being referred for surgery.

The diagnosis of retinal detachment is frequently easy, though holes or tears without detachment may be difficult to detect. The symptoms of flashes of light or a shower of vitreous opacities must be carefully evaluated. The recognition of a preclinical detachment and its prompt treatment definitely improves the prognosis. Indirect ophthalmoscopy and scleral depression are useful adjunctive tools in recognizing peripheral tears or holes.

The operative treatment of retinal separation necessitates a thorough knowledge of the fundus and the location of the holes. Unless the holes are surrounded with diathermy applications, the operation is usually unsuccessful. It is imperative to have good ophthalmoscopic control of the operative procedure.

One of the most annoying complications is to be unable to obtain subretinal fluid. This usually occurs in fairly flat detachments of long duration. The injection of air or saline is recommended in cases in which the retina is considerably elevated at the conclusion of the operation, or if one suspects retraction of the vitreous.

In the postoperative period several events may occur. The retina may settle back and become firmly reattached, or it may settle

back and redetach in a contiguous area or in a diametrically opposite area of the globe.

In the first instance it is likely due to failure of closure of a hole or the development of a new one. In the second instance it may be due to contracture of a vitreous band.

The retina may settle not at all, or only partially. This may be due to failure to close the hole or to contracture of the vitreous.

Finally there may be actual progression of the detachment. This is believed to result from massive vitreous contracture.

The two most important factors in failure of detachment surgery are believed to be failure to localize and close the hole and retraction of the vitreous.

Discussion. Dr. Isadore Givner asked whether, in an aphakic eye, there is any advantage in injecting air into the anterior chamber instead of into the vitreous.

Dr. Frederick Theodore asked the age of the oldest patient on whom Dr. McDonald had successfully operated for this condition.

Dr. Levitt asked if Dr. McDonald had any experience with any of the scleral shortening operations.

Dr. Sitchevska asked how to manage retinal detachment after vitreous hemorrhage in an only eye.

Dr. Smith mentioned that the release of subretinal fluid is very important.

Dr. McDonald replied to Dr. Givner that he prefers injecting air into the anterior chamber if the hyaloid is intact. If the hyaloid is not intact, it makes no difference if air is put into the anterior or posterior chamber. The one objection to this procedure is that the air obscures the fundus.

To Dr. Theodore, Dr. McDonald said that the oldest patient he had successfully operated was in the seventies; it was the second eye operated for detachment, the first eye was operated 15 years previously, also with successful results. Dr. McDonald said that he often finds symmetrical defects in the periphery of both eyes. As regards scleral resection, in a series of 123 cases, five patients had scleral resection—one successfully—as the primary procedure. The balance of the group all had had two or three previous operations.

Regarding the management of a patient with vitreous hemorrhage in his only eye and a detachment of the retina, Dr. McDonald suggested waiting until the hemorrhage clears before operation. He said that operating without seeing the hole usually causes trouble. If there is a good history as to where the hole is, a good operation in that quadrant may be possible.

Dr. McDonald said that he agreed with Dr. Smith that draining of the subretinal fluid is good especially in large bullous detachments.

Retrolental fibroplasia

Dr. William C. Owens (Baltimore) said that certain facts have been established about retrolental fibroplasia. The disease occurs primarily if not exclusively in premature infants. Both eyes are affected during the acute phase. It is either an entirely new disease or a disease that has had a marked increase in its incidence during the last 15 years.

The clinical course of the disease has been clearly described. The major clinical manifestations from the first evidence of fundus abnormality to the appearance of a retrolental membrane usually occur between the first and fifth month of postnatal life.

The acute phase of the disease may be divided into three stages:

(1). The early stage of dilatation and tortuosity of the retinal vessels with the formation of capillary aneurysms.

(2). The appearance of localized or generalized grayish retinal elevations and retinal hemorrhages.

(3). The extension of the new vessels and supporting tissue from the retina into the vitreous with detachment of the retina.

About 55 percent of all premature infants weighing three pounds or less at birth show some evidence of the acute phase of the

disease. However, the disease is self-limiting and in many infants showing the acute phase there is a spontaneous regression.

The extent of destruction seen in the late cicatricial stage depends upon the severity of the acute phase and the amount of regression which has occurred. The late cicatrical stage may show a great variety of pictures from the formation of a complete retrolental membrane in a small stunted eye to minimal residua such as myopia with a few retinal scars.

The pathologic picture of the disease is characterized first by the proliferation of capillary endothelium to form small aneurysms and abnormal buddings in the nerve-fiber layer of the retina. Surrounding the areas of capillary proliferation are increased numbers of glial cells. This is followed by the formation of areas of edema and hemorrhage in the greatly thickened nerve-fiber layer. As the disease progresses the newly formed capillaries extend from the retina into the vitreous surrounded by fibrous tissue network resembling retinitis proliferans. Retinal detachment follows.

In contrast to these established facts on the clinical course and the pathologic aspects of retrolental fibroplasia, there is still no knowledge of the etiology of the disease, and conflicting reports exist on the methods for its prevention or treatment.

Discussion. Dr. Vesey asked if there is any history of consanguinity. Dr. Owens replied that there is no Rh factor or history of consanguinity.

Dr. Smith asked if there is any time factor in the development of the three stages; to which Dr. Owens answered no. The disease picture may change from normal eyes to complete Stage 3 in two or five months.

Dr. Lisman asked beyond what age will the baby not develop retrolental fibroplasia. Dr. Owens said that, if examination is negative after the age of three months, the chances are that nothing will develop. On the other hand, the condition might be present, recede, and then start up again.

Dr. Agatston asked at what age do cataracts develop. Can there be membrane formation which regresses? How often are the discs seen through the membrane? Dr. Owens answered that membranes never subside, and can recede only if the condition goes back to Stage 3 (retinal involvement). Visualization only occurs if the membrane is incomplete. Cataracts form late, at about six to eight months, and involve the nucleus and cortex.

Bernard Kronenberg,
Recording Secretary.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

February 21, 1952

Dr. George F. J. Kelly, M.D., *chairman*

Regression of breast carcinoma following sterilization

Dr. Richard Ellis (by invitation) and Dr. Harold G. Scheie reported two patients with metastatic lesions from breast carcinoma which showed marked regression following sterilization by X ray. Metastasis to the choroid was present in the left eye of one of these patients and both eyes of the other.

The prognosis for patients with carcinoma of the breast, who have developed distant metastasis, such as in the lungs or eyes, is considered hopeless. Radical excision of the primary tumor with or without local X-ray therapy may be indicated. This usually has no effect upon the metastasis.

Recent developments in therapy, however, have shown some promise in retarding the course of the disease. Among these measures in treating metastatic breast carcinoma are the use of hormones and castration. While the modes of action are unknown, it has been noted that alteration of the hormonal status

of the individual by sterilization or hormonal therapy may profoundly influence the course and the character of advanced breast carcinoma.

Castration is most effective in premenopausal women and at menopause if there is evidence of residual ovarian activity. Surgical removal of the ovaries and irradiation to the ovaries are the two methods employed for castration.

After castration, there is a remission in 20 to 40 percent of the cases. Lung metastasis and soft tissue lesions regress and osseous lesions calcify. The duration of remission following castration may last from a few months to several years. The untoward effects are menopausal symptoms which can be controlled with testosterone.

CASE 1 is that of a 31-year-old nurse who came to see Dr. Scheie in July, 1949, because of blurred vision in left eye. Two years previously she had a radical mastectomy for adenocarcinoma of the breast. Her vision was 6/6 in the right eye, and corrected to 6/15 in the left.

Ophthalmoscopic examination revealed a normal right eye. However, the left fundus presented a typical metastatic lesion with four diopters of elevation at one point. In view of the past history and the fundus lesion, a diagnosis of metastasis to the eye from breast carcinoma was made, and the patient was admitted to the Hospital of the University of Pennsylvania. A thorough survey revealed a number of small dense nodules probably representing metastasis in the chest. For several reasons following a consultation with two other ophthalmologists, enucleation of the eye was advised.

On August 26, 1949, the left eye was enucleated. (The first slide is a photomicrograph of the globe showing metastasis to the choroid from carcinoma of the female breast with a moderate degree of invasion of the choroid. The appearance of the tumor was similar to the breast carcinoma obtained from the same patient.

The patient was told that for reasons of precaution, sterilization should be performed. Therefore, a sterilizing dose of radiation to the ovaries was started on September 2, 1949. Following this procedure, the densities of the lung entirely disappeared.

(A photograph of the X-ray studies before treatment, showing small shadows in the upper lobes interpreted as metastatic sites, was shown. The next slide showed the clearing up and no evidence of metastasis.

The patient had no further difficulty until recently, when it was thought she had recurrences of lesions in the lungs.

CASE 2. The second patient was a 40-year-old white woman who had a radical mastectomy for breast carcinoma in September, 1949. Ten months later she consulted Dr. Scheie because of blurring of vision.

Examination of the eyes revealed bilateral, rather typical lesions thought to be due to metastasis from breast carcinoma. The top of the lesion in the right eye was elevated eight diopters, and the left eye was slightly less elevated. Her best corrected visual acuity was 6/15 in each eye.

A study at the Hospital of the University of Pennsylvania demonstrated metastatic lesions involving both lungs, skull cervical spine, ribs, pelvis, and femora. She also had recurrent subcutaneous nodules in and around the mastectomy scar.

A sterilizing dose of X ray was given. Examination three months later revealed that the skin nodules in the mastectomy scar had disappeared. There was also regression of the metastatic lesion in the lungs and bones, and ocular lesions had cleared entirely, leaving scattered areas of retinal atrophy.

(A slide, showing the chest X-ray picture prior to treatment, was described by the radiologists as being typical of metastatic carcinoma. The next slide was an X-ray picture three months later, showing definite evidence of improvement.)

In about three months, however, the patient suffered a relapse and died eight months later despite treatment with testosterone.

In conclusion, we have reported these patients with metastatic carcinoma of the breast who were treated by sterilization, because of the rather remarkable clearing of the chest lesions in both patients, and the ocular lesions in both eyes of one patient. To the best of our knowledge, this latter observation has never been recorded.

Discussion. Dr. Harold G. Scheie discussed one phase of the management of the first patient mentioned by Dr. Ellis. Many of you may have questioned the advisability of enucleating the left eye which showed only a relatively small lesion of metastatic carcinoma.

The problem was an interesting one. The patient had been seen by two other ophthalmologists who, knowing her history of mastectomy, had withheld their true diagnosis. They told her, instead, that she had retinitis. She was, however, well aware of the possibility of metastasis because she had been told of the malignancy in the breast.

She telephoned our office on a Sunday night to arrange for a consultation for the following morning. She falsified her history, and denied any ill health including past surgery. In fact she stated she had gained weight in the past two years. This was probably true because more than likely she had been underweight at the time of amputation of her breast.

Thinking in terms of a primary neoplasm and the need for having thorough studies made, I told her that I believed there was something in back of the eye that should not be there. She brought up the question of a growth, and I said there was a possibility. At that point she revealed the previous surgery and the diagnosis of the carcinoma of the breast.

We admitted her to the hospital where study revealed metastatic lesions in the lung in addition to the ocular lesion. Knowing her life expectancy was reasonably a matter of several months, and hoping to relieve her anxiety, we told her that we thought the eye might represent the only metastatic lesion in her body and for this reason advised enucleation. We believe this was justifiable, because she has had two and one-half useful and relatively happy years since that time.

Dr. Henry L. Birge asked Dr. Scheie what his experience has been with metastatic lesions in the eye from the lung, and does sterilization do any good in this type of lesion? To which Dr. Scheie replied that Dr. Ellis and he had seen no patients with metastasis to the eye from the lung. Dr. Ellis might want to correct me, but I doubt that hormonal therapy of the type mentioned in this paper would have any effect upon a tumor that had its primary source in the lung.

Little is known about how hormonal therapy does exact its effect upon metastatic lesions from the breast. It seems possible that the ovaries during the menstrual cycle stimulate breast tissues to grow. Sterilization eliminates that factor. I do not know of any influence that it might have upon primary lung tumors.

Retinal arteriolar changes in hypertension

Dr. Glen Gregory Gibson: The interpretation and classification of the retinal arteriolar signs of hypertension is one of the most important and difficult problems in ophthalmology today. The signs occur with sufficient consistency to permit diagnostic and prognostic evaluations which have stood the test of time.

The three most significant signs are generalized narrowing, focal spastic and sclerotic narrowing, and generalized sclerosis. Each of these signs may be divided into four grades, each of which represents increasing degrees of involvement.

The retinal arteriolar signs are quite dissimilar in those patients whose hypertension pursues a relatively rapid course, from those whose hypertension runs a chronic course. The more active forms of the disease are associated with the various grades and types of arteriolar narrowing changes, while the alteration in the arterioles in the more chronic

type is characterized by no, or very slight, narrowing. If patients were properly classified on the basis of their retinal arteriolar findings, the ultimate solution of this problem might be hastened.

Discussion. Dr. Paul Kahn, Jr.: I would like to ask Dr. Gibson about arterial straightening. What is its pathogenesis and what is its significance in the fundus examination in hypertension?

Dr. George F. J. Kelly: When a vessel appears narrowed, how can you tell whether this is due to hypertension or to a sclerotic thickening of the walls?

Dr. Henry L. Birge: One of Dr. Gibson's basic hypotheses is the relation between the veins and the arterioles. The normal relationship, he states, is to have the arterioles two thirds of the size of the vein.

I would like to emphasize the importance of the size and color of the veins. In cases of polycythemia, right heart failure, and increased cerebral venous pressure, the veins are all distorted and the grade of narrowing of the arterioles has to be estimated on the observers' remembrance of what is a normal arteriolar-vein relationship.

Clinically, the importance of arteriosclerosis is well known. But arteriosclerosis is usually associated with other abnormalities. For instance, retinal venous thrombosis may have both arteriosclerosis and venous diseases and blood diseases as etiologic factors.

If we are to make adequate diagnoses and to use our diagnostic acumen to prevent complications, we must make use of each and every significant fact.

Sometimes the importance of changes in the retinal veins are not easily understood. We have recently been impressed with the great value of checking the blood elements in all their component parts. We have found more cases of relative polycythemia than are generally believed to exist.

The point I am making is that changes in the veins are just as important as changes in the arterioles, and that sometimes we need additional tests to help estimate the meaning of venous changes. I wonder if Dr. Gibson has found an increased incidence in venous and blood diseases from his studies of the retina and whether he has found it valuable to make more use of the blood-volume tests?

Dr. Glen G. Gibson: This story of hypertension as it has been unfolded represents the essential concept attained by clinical ophthalmoscopy. Unfortunately, it is not based on microscopic evidence. Optical or refractive factors may affect the appearance of retinal arterioles and many of the changes so seen do not show in microscopic section. It must be understood that many of these statements are based on inference, and almost all of them are open to some objections. The terminology is unsatisfactory. There is much work to be done on it.

The first question concerned the significance of straightening. I am not prepared to answer that question, because I thought the question would be on tortuosity. One of the most misleading and unreliable signs is tortuosity. It occurs and is a sign of hypertension. It occurs particularly in the small arterioles which normally increase in visibility in the vicinity of the macula. However, since it does not occur with any consistency, it is not a very reliable sign.

Arteriolar straightening may be a sign of hypertension. In hypertensive patients, the normal undulation of a vessel tends to become diminished so that the vessel becomes straighter. That is not a reliable sign, and it is not of much prognostic significance. It is probably due to fibrosis and contracture in the media of the arteriolar wall.

Dr. Kelly has asked how to tell hypertensive narrowing from some of the other types of narrowing, such as occur with sclerosis and thickening. It must be admitted there are some errors in the interpretation of these findings, and this is why the subject is not easy for internists or general practitioners. They do not understand the changes which may occur in high myopia, in astigmatism, and in hyperopia—all of which have a modifying effect on the fundus appearance.

There are some people who have normally small vessels, and there are some who have normally large vessels, and that must be taken into the interpretation. In other words, the diagnosis of hypertension cannot be made merely on the size of the vessel; the picture of the venous and arteriolar systems as a whole must be considered.

The differentiation between hypertensive narrowing and sclerotic narrowing is that, in the hypertensive narrowing, the vessel appears uniformly narrowed. It is much more marked at the periphery of the arteriole and that tends to diminish toward the discs.

Dr. Birge has asked how to tell whether a patient with polycythemia has hypertension? I think that is one of the most difficult questions I have ever had to answer. Aside from being difficult, this combination rarely occurs, and I will be happy to miss the diagnosis in all those patients who have both diseases.

Miotic-resistant pupil

Dr. George S. Tyner (by invitation) and Dr. Harold G. Scheie said that mydriasis is one of the characteristic clinical signs of acute narrow-angle or congestive glaucoma. It has long been known that, in certain instances, treatment with miotics of any type fails to bring about miosis or reduction in the intraocular pressure. Therefore, fulminating attacks, which require surgery must be operated under adverse circumstances.

This paper is a report of investigations undertaken to determine the mechanism responsible for the miotic-resistant dilated pupil of acute glaucoma and to present certain conclusions regarding its origin.

The most likely explanations are: (1) Sympathetic irritability; (2) pressure paresis of the motor nerves to the iris sphincter as they pass through the suprachoroidal space; (3) a disturbance of the local neurohumoral mechanism; (4) the effect of pressure upon the muscle cells of the iris sphincter rendering them incapable of contraction.

The first explanation, sympathetic irritability was ruled out by clinical observations of one of us (H. G. S.). After miotic drugs had failed to produce miosis in patients with acute attacks of glaucoma, the superior cervical ganglion was injected with procaine. All the clinical signs of a classical Horner's syndrome were produced except miosis. The pupils remained dilated.

In order to investigate the other three possible explanations, a simple apparatus was devised to produce artificial elevation of the intraocular pressure in dog eyes. Preliminary experiments indicated that the second explanation, pressure paresis of the motor nerves as they pass through the suprachoroidal space, was not the mechanism responsible for the mydriasis.

When the intraocular pressure was raised to levels ranging from 40 to 60 mm. Hg (Schiøtz) in normal dog eyes, the pupils dilated. As long as the pressure was kept in this range, the pupils remained dilated. The mydriasis was resistant to miotics whether of the cholinesterase-inhibiting type, such as DFP and eserine, or drugs which act upon the motor end-plate or muscle cell directly, such as acetylcholine, pilocarpine, and mecholyl. If pressure paresis of the nerves with resultant decrease in output of acetylcholine were the explanation, the pupils should have constricted with pilocarpine or mecholyl.

We attempted to study these pupils at different levels of intraocular pressure and variable times during which the pressure was elevated. We found that either type of miotic agent would produce miosis until the pressure was sufficiently high to produce pupillary dilatation. Likewise, when the drugs were used separately or in combination prior to raising the intraocular pressure, the pupils still dilated at the critical level of 40 to 60 mm. Hg.

For further evidence against the theory of pressure paresis of the motor nerves to the sphincter iridis, experiments were done on denervated pupils. In different sets of experiments, the ciliary ganglion was removed

or blocked, thereby eliminating the postganglionic parasympathetic motor-nerve supply.

The pupil was then constricted by pilocarpine. When the intraocular pressure was elevated to levels between 40 and 60 mm. Hg, the pupils again dilated. When the pressure was reduced below 40 mm. Hg, the pupils again constricted with pilocarpine. This likewise occurred in one animal in which the third nerve had been cut surgically through an intracranial approach.

Finally, we attempted to investigate the last two explanations, disturbance of the local neurohumoral mechanism at the motor end-plate and the effect of pressure on the muscle cells.

Since calcium ions stimulate the muscle cell itself, 0.3 cc. of aqueous was replaced by a solution of 10-percent calcium gluconate. Miosis of one to three mm. promptly resulted. When the intraocular pressure was rapidly raised to levels approaching 70 mm. Hg by injection of air into the vitreous cavity, pupillary dilatation occurred rapidly in all eyes.

Thus, it seems apparent that the muscle cells themselves are incapable of contracting when the intraocular pressure is elevated high enough to reach the critical level between 40 and 60 mm. Hg.

In summary, it seems apparent from these experiments that the dilated, miotic-resistant pupil, produced by experimentally increasing the intraocular pressure of the dog eye, results from the effect of pressure upon the cells of the sphincter muscle of the iris. We cannot state with certainty whether this effect is due to the pressure on the muscle itself or whether the pressure in some way interferes with the blood supply or the nutrition of the muscle.

Discussion. Dr. Harold Scheie: Dr. Tyner has presented evidence which indicates that mydriasis due to increased intraocular pressure occurs as a result of depression of the muscle itself. One point not mentioned in the production of this miotic-resistant dilated pupil is failure of the miotic drug to be absorbed.

The experiments described by Dr. Tyner, however, showed that pupils previously constricted by pilocarpine, or even by calcium ions, dilated promptly with elevated intraocular pressure. We also know that patients may have acute attacks of glaucoma while being treated with miotics. The pupil then dilates during the attack. We believe there is considerable evidence for believing that disturbance with the blood supply of the sphincter iridis may be at fault.

We have examined the eyes of patients having had acute glaucoma, who are being followed in a glaucoma clinic at the Hospital of the University of Pennsylvania, and found that a fairly significant percentage had rather severe marginal iris atrophy near the pupillary border, which might well result from ischemia.

The increased intraocular pressure could conceivably compress the iris, thereby preventing any possible flow of blood into the iris; or by localized pressure back of the iris compress the vessels against the trabeculum.

The canal of Schlemm is a filter which might be thought of as a sink trap. As with a sink, a rubber dam or sheet of paper in the water draining through the trap, providing it was large enough, might cause obstruction and pressure build-up behind it.

The analogy can be applied to the iris during acute attacks of glaucoma, when the aqueous accumulates posteriorly. Pressure is localized to the iris periphery in the region of the trabeculum and, as a result, the blood supply which comes from the greater circle is obstructed at this point, and the iris is rendered ischemic.

M. Luther Kauffman,
Clerk.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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THE REGISTRY OF OPHTHALMIC PATHOLOGY

The establishment of the Registry of Ophthalmic Pathology at the Army Medical Museum just 30 years ago was the concrete expression of widening interest in pathology of the eye. The late Dr. Harry S. Gradle, representing the ophthalmologists in the membership of the American Academy of Ophthalmology and Otolaryngology, and Maj. George R. Callender, then the curator of the museum, representing the pathologists, organized to pool their material and knowledge to create a center for eye pathology in America. Important contributions to the subject had been made before that time from the few existing centers of ophthalmology in this country, but ophthalmologists at large were little interested in pathology and general pathologists were equally little concerned with the eye.

The registry almost immediately had the effect of promoting interest in ophthalmic pathology, and its signal success provided a stimulus for the subsequent development of a broader registry program. The early

hope that a demonstration of the value of such a center would encourage the foundation of ophthalmic pathology laboratories throughout the country is now being realized. The American Academy of Ophthalmology and Otolaryngology has never wavered in its support of the program for ophthalmology and, in 1935, was instrumental in the establishment of a Registry of Otolaryngic Pathology. This was also one of the earlier registries, now numbered among the 21 comprising the American Registry of Pathology, one of the five departments of the Armed Forces Institute of Pathology.

The plan to utilize the best of the contributed material to make up study sets of microscopic slides with syllabuses containing clinical histories and supplemental data proved so popular that the compilation of the early atlases of ophthalmic and otolaryngic pathology were the logical steps in the progress of this venture. The slide study sets and atlases are, of course, part of the educational function of the Registry; the courses in eye pathology given at the Armed Forces Institute of Pathology and at medical centers throughout the country and abroad represent direct instruction. Although these are designed primarily for ophthalmologists in the Armed Forces, civilians in as large numbers as possible are also enrolled. These courses have fostered interest in pathology of the eye among many of the younger clinicians.

So great an accumulation of material (35,000 enucleated eyes, biopsy specimens, and slide preparations) as that in the registry provides not only a wealth of teaching material but also an exceptional opportunity to any qualified research worker in the country. As early as 1931, Callender was able to suggest a classification of melanomas of the uveal tract, based on histologic characteristics, from his study of 111 cases followed five years or longer. Four years later, in collaboration with Wilder, this work was carried further to include an evaluation of fiber content in relation to prognosis. By 1942, Callender, Wilder, and Ash reported a study of 500 uveal melanomas followed five years or longer in which the prognostic value of such histologic characteristics as cell type and fiber content was firmly established. In 1951, Wilder and Paul, in a study of the 2,535 uveal melanomas registered, were able to demonstrate the validity of classification by cell type and fiber and pigment content in 1,064 cases followed five years or longer, 598 of them for 10 years or more.

The most recent investigative project to emerge from the registry throws new light upon the obscure etiologic factors in granulomatous chorioretinitis. For years, because of the character of the inflammatory process, the lesions have been regarded as tuberculous or, in the presence of a positive Wassermann reaction, as syphilitic, but the causative organisms have seldom been identified in the lesions. In reëxamining these cases, Wilder demonstrated protozoa indistinguishable from toxoplasma in 30 of 131 cases carrying the pathologic diagnosis of tuberculosis, and in 23 others with that of syphilitic chorioretinitis and chorioretinitis of unkown etiology. The organisms are seen in necrotic portions of the retina as crescentic forms, often in pairs, or as spherical forms occupying pseudocysts. They are best preserved in celloidin sections, whereas, in paraffin sections, they are shrunken and distorted and difficult to distinguish from nuclear debris. This doubtless explains why they have been overlooked for so long. With the oil immersion lens the organisms were readily found in hematoxylin-eosin stained sections from about half the cases, but careful search was required in the other half. The identification of a specific organism in such a large group of cases of chorioretinitis presents the possibility of treatment, particularly if clinical tests in the early stages of the eye disorder indicate the presence of toxoplasmosis.

Such studies as these are stimulated by a

great concentration of pathologic material; this in turn implies large numbers of interested and generous contributors, not only of selected material but also of ideas. Material is gathered not with a view to establishing a static collection for which numerical superiority can be claimed or from which only statistical studies emerge. The collection is in constant use for the assembly of study sets, the preparation of atlases, and for continuing research. After the establishment of the pathologic diagnosis, the material within certain disease categories is restudied in the hope of clarifying obscure concepts and gaining information of practical value to all those engaged in the practice of ophthalmology. The aim of the Registry of Ophthalmic Pathology, as well as all other registries, is to return, not in kind, but in value, the contributions of those whose generosity has made the program possible. This return can best be made in the form of teaching material and in the opportunities offered for research directed toward the solution of the many problems posed by ocular disease.

Elbert DeCoursey.

OPHTHALMOLOGY AND THE AMERICAN COLLEGE OF SURGEONS

The 38th Clinical Congress of the American College of Surgeons in New York City, September 22 to 26, 1952, was featured by a large attendance and an increased interest in the ophthalmic program.

The program for ophthalmology was well planned and consisted of panel discussions in the mornings and symposia in the evenings. Approximately 200 ophthalmologists attended the symposia and about half that number participated in the panel discussions. The meetings were held Tuesday, Wednesday, and Thursday in the Waldorf-Astoria and the Belmont Plaza.

Panel discussions on "Problems concerned with extraction of complicated cataracts," with Dr. John H. Dunnington as moderator, created considerable interest on the opening day. Dr. Walter S. Atkinson, Dr. Henry L. Birge, and Dr. Glen Gregory Gibson participated in various phases of the program.

An evening symposium on "Surgical correction of motor anomalies involving extraocular muscles" was directed by Dr. Edwin B. Dunphy. The following participated: Dr. Harold W. Brown, Dr. Harold G. Schie, Dr. Walter H. Fink, and Dr. Raynold N. Berke. A total of 235 ophthalmologists attended this session. The audience stood in silence in honor of the late Dr. Richard G. Scobee, who was selected originally to present a part of the program.

A discussion on "Orbital implants" with Dr. Arno E. Town as moderator was held on Wednesday morning. The collaborators were Dr. Alston Callahan, Dr. John P. Macnie, and Dr. Raymond E. Meek. The evening session was a symposium on "Causes of failure in ocular surgical procedures," with Dr. Wendell L. Hughes presiding. Others taking part in the program were: Dr. Brittain F. Payne, Dr. Joseph A. C. Wadsworth, Dr. Daniel B. Kirby, Dr. Truman L. Boyes, and Dr. P. Robb McDonald.

The program for Thursday consisted of a panel discussion on "Fallacies in refraction by use of mechanical refractors" with Dr. Conrad Berens acting as moderator. Dr. Alfred Cowan, Dr. Arthur Linksz, and Dr. Daniel Snydacker opened the discussions. The evening session was conducted by Dr. Frederick H. Verhoeff with the following participants: Dr. Harold H. Joy, Dr. George M. Haik, Brig. Gen. Elbert DeCoursey, Dr. David G. Cogan, Dr. Raymond L. Pfeiffer, Dr. Norman L. Cutler, Dr. Robison D. Harley, and Dr. Hedwig S. Kuhn. The subjects discussed were: "Sympathetic ophthalmia," "Atomic eye injuries," "Management of intraocular foreign bodies," and "Treatment of eye burns."

The success of the program was largely due to the time, effort, and thought devoted

to its planning by the officials of the congress and the program committee. If this high standard is continued, ophthalmology will assume a more important role in functions of the American College of Surgeons.

Brittain F. Payne.

XVII INTERNATIONAL CONGRESS OF OPHTHALMOLOGY

September 13 through September 17, 1954
New York City
Waldorf-Astoria Hotel
Subjects for discussion: *Glaucoma* and *Uveitis*

CORRESPONDENCE

Alternating hypertropia

Editor,
American Journal of Ophthalmology:

In Dr. Schlossman's article on the "Significance of alternating hypertropia" in the June, 1952, issue of the JOURNAL, there are a few statements which are rather puzzling. The statement that "the difference between hyperphoria and hypertropia is largely one of degree" is open to question. A phoria is a tendency to deviation which is held in check by the fusion faculty, whereas a tropia is an actual deviation with the fusion faculty inactive. It is true that a phoria, say a hyperphoria, may at times become manifest and show itself as a hypertropia, but the basic difference that one is a tendency to deviation (a latent condition) and the other an actual deviation (a manifest condition) is still there.

More important is the bearing of this in a compound imbalance. The author, perhaps unwittingly, says in effect that one can have an esotropia (slight esotropia) combined with a hyperphoria. How is this possible? One can have an esotropia with a hypertropia, that is a manifest deviation of the eye turning up and in. But if one has a manifest deviation inward, an esotropia with the fusion faculty inactive, what would prevent a tendency to turn upward, a hyperphoria, from becoming manifest and showing itself as a hypertropia?

(Signed) Joseph I. Pascal,
New York.

Dr. Schlossman's reply

Editor,
American Journal of Ophthalmology:

Dr. Joseph I. Pascal takes exception to my statement that "the difference between hyperphoria and hypertropia is largely one of degree." While I realize that there are differing opinions on this subject, I believe that the above statement is essentially correct. When there is a tendency to deviate, the deviation may become manifest at any time due to a wide variety of conditions such as fatigue, onset of presbyopia, and so forth.

In our study "Role of heredity in etiology and treatment of strabismus" (A.M.A. Arch. Ophth., **47**:1-20 (Jan.) 1952), Dr. Bruno S. Priestley and I have shown that one member of a particular family may have a heterophoria while another person in this family may have a heterotropia; however, the direction of the anomaly is the same, namely convergent or divergent. It is obvious that the person with heterophoria had a similar genetic background to that of the patient with heterotropia. Finally, there are numerous patients with intermittent strabismus in whom under varying conditions both heterophoria and heterotropia are present.

In answer to the query in the second paragraph of Dr. Pascal's letter, I would like to quote the following passages from my paper: "Although the term hyperphoria is usually used in referring to this type of case, it was felt that, since the primary lesion is an esotropia, the vertical imbalance is similarly a hypertropia. When the vertical deviation is minimal, it is sometimes extremely difficult

to determine whether one is dealing with a hyperphoria or a hypertropia."

Incidentally, Dr. Pascal states that the fusion faculty is inactive in strabismus. Since many patients with squint show a certain amount of fusion, I think that it would be more accurate to refer to a defective fusion faculty than to an inactive one.

(Signed) Abraham Schlossman,
New York.

BOOK REVIEWS

ULTRAVIOLET RADIATION. By Lewis R. Koller, Ph.D. New York, John Wiley and Sons, 1952. 270 pages with numerous illustrations and figures, references, and index. Price: $6.50.

Dr. Koller has clarified the vast complex data relating to ultraviolet in a readable, neatly organized presentation, crammed with precise documented facts, much of which is of direct ophthalmic interest. The visibility curve at the ultraviolet end of the spectrum is extremely steep, the sensitivity to 3,650 A being only 1.5 percent that of 4,047 A. The crystalline lens of youth permits perception as far as 3,130 A, and the sensitivity of the aphakic, at 3,650 A, is about one thousand times that of the normal adult. Erythema is most effectively produced at 2,967 A, but at 2,800 A the conjunctiva is more susceptible than the skin because of the absence of a strongly absorbing horny layer.

Finsen, who in 1899 discovered that the ultraviolet of sunlight is responsible for sunburn, received the Nobel prize in 1903 for his work in ultraviolet therapy. Most of the solar ultraviolet is absorbed and scattered by the atmosphere so that natural ultraviolet shorter than 2,863 A has not been encountered. The scattering accounts for the blue of the sky which is thus endowed with ultraviolet radiation comparable to that received directly from the sun. Pigmentation without erythema results from wavelengths greater than 3,200 A—a finding utilized practically in protective suntan lotions and creams.

Ultraviolet lamps are specially designed for specific purposes. Rays shorter than 2,800 A are excluded from therapeutic lamps and their weaker models, "sun-lamps"; for illumination the cut-off is at 3,000 A; while germicidal lamps have their greatest efficiency at 2,537 A, and for fluorescent effects 3,650 A is optimum. The advantages and disadvantages of the different types of lamps in these fields are thoroughly discussed, as well as everything else of ultraviolet significance.

James E. Lebensohn.

TRANSACTIONS OF THE PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY, 1951.

A number of discussions recorded in this volume are of ophthalmic interest. Oscar Hirsch, in an essay on the symptoms and treatment of pituitary tumors, briefly reviews the anatomy of the region, the classification of the tumors, ocular symptoms, X-ray findings, and differential diagnosis and discusses the methods and results of surgical treatment more extensively.

Bruce Fralick gives much useful advice in an extensive discussion of the management of complications after cataract extraction. His opinion based on wide experience and the capacity to evaluate it are most helpful.

Merrill J. Reeh describes three unusual cases of melanoma of the iris and ciliary body. In one in which the entire iris, trabeculum, and ciliary body were infiltrated with cells that had also invaded the choroid as far back as the equator, the patient had noticed a change in the color of his iris from blue to brown two years before. The two other cases emphasize the importance of knowing that malignant melanoma does occur in young patients. In one case, a sudden intraocular hemorrhage called attention to discrete tumor, but gonioscopic examina-

tion showed that it extended back into the ciliary body. It was this datum that made enucleation rather than iridectomy seem advisable.

Homer Smith reports three additional cases of aplasia of the optic nerve. The eyes were otherwise normal but a review of the literature bears out the statement of Cordes that the condition is rare in otherwise normal human eyes.

Nugent and Higgins discuss the relation of nutrition to the eye. Four types of cataracts may be produced by altered nutrition but their origin has not been explained. Dudley Bell calls attention to the value of iontophoresis. It is an excellent method for the prompt administration of drugs into the cornea, aqueous, iris, and ciliary body.

A. Edward Maumenee and Raymond C. Michler point out that the operative area in ocular surgery cannot be sterilized. They suggest a method for the preparation of the field.

James R. Powell reports four cases of episcleritis and scleritis in four of which the response to local treatment with cortisone was dramatic. He discusses their relation to the collagen disease and the place of cortisone in the treatment of diseases of the eye.

Talbot and Christensen point out that it is probable that two of three eyes enucleated after previous intraocular surgery will show significant amounts of intraocular foreign substance if examined with polarized light. The sponge is a great source of contamination and gloves, drapes, and irrigating fluids contribute significant amounts.

F. H. Haessler.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF NEW ZEALAND, 1951.

As part of his address as president, L. S. Talbot discusses the problems of diagnosis and management and describes eight cases which emphasize the importance of the utmost care and alertness. Malignant disease is far more commonly associated with retinal detachment than he had at one time thought.

Bruce H[illegible]ilton discusses the Australian program for the prevention of blindness. The sight-saving school actually does save sight. Three glaucoma clinics have been set up in Australia and the problems of rubella in pregnancy, toxoplasmosis, retrolental fibroplasia, and the eye hazards of industry receive adequate consideration.

G. A. Pittar, who discusses the treatment of conical cornea by corneal grafting, believes that grafting should be considered as soon as vision is bad enough to warrant it in patients who do not tolerate contact glasses. One should not wait until it is certain that the process is stationary.

Rowland P. Wilson gives a most interesting illustrated account of artificial eyes in ancient Egypt. The very beautiful and perfect eyes were used in mummies and mummy masks, coffins, and statues and probably never in the living.

Walter J. Hope-Robertson was delighted by the generous welcome he was given in the continental as well as British clinics which he visited when attending the XVI International Congress in 1950. His hosts exposed him to a wealth of interesting experience.

Barrie Jones reports a case of human myiasis due to Oestrus ovis; Graeme Talbot describes unusual eye injuries; Rowland P. Wilson contributed a brief discussion on the relation of the eyes to headache; and Howard Coverdale briefly calls attention to macular edema.

A. C. Sandston draws attention to the problems of orbital implantation as a means of correcting cosmetic defects after enucleation of the eye, and D. S. McKenzie reports a family tree of six generations with 19 cases of retinitis pigmentosa.

F. H. Haessler.

TRANSACTIONS OF THE AMERICAN OPHTHALMOLOGICAL SOCIETY, 1951. New York, Columbia University Press, Volume 49.

The American Ophthalmological Society held its 87th annual meeting at White Sulphur Springs on June 7, 8, and 9, 1951; 22 papers were presented and discussed; six theses are published in the transactions.

A case report of a new progessive type of choriopathy is recorded by A. J. Bedell. The ocular pathology of polyarteritis nodosa with early histopathologic findings is discussed by E. L. Goar and L. B. Smith.

G. V. Simpson describes three cases of opacities in the vitreous which are assumed to be detached pieces of the retina. The symptoms are flashes of light, an irregular shaped floater, and haziness of vision. The prognosis is good.

Algernon Reese finds a frequent association of iris nevi with ipsolateral skin nevi or neurofibromatosis. The recognition of the true nature of a pigmented iris lesion is essential in determining the best course of treatment. An atypical case of suprasellar meningioma is reported by H. H. Joy.

During a symposium on cataract C. D. Townes, C. T. Moran, and H. A. Pfingst reported a series of 560 cataract operations. There were postoperative complications in 80 which delayed or prevented the restoration of useful vision. H. F. Hill after a careful study of 401 cases of cataract extractions performed with the keratome-scissors incision concludes that this technique is preferable to the Graefe-knife incision. F. B. Fralick and R. M. Fox, from data on 187 cases of complicated cataract, find that the visual results in 62 percent were 6/9 or better and in 38 percent an acuity of 6/12 or less.

Parker Heath reports the histopathology of 19 neuro-ectodermal tumors of the iris. The local removal, properly performed, is usually successful. Derrick Vail and E. H. Merz present a case of embryonic intra-epithelial cyst of the ciliary process. Such cysts may remain small and symptomless or develop into larger cysts requiring removal of the eye.

Terramycin in ocular infections is ineffective against the viruses of vaccinia and herpes simplex. The results in trachoma are questionable. Also Phillips Thygeson finds it effective against a large range of bacteria. Terramycin has low sensitizing properties.

Jonas S. Friedenwald, W. C. Owens, and E. U. Owens describe the pathology of "Retrolental fibroplasia." The earliest changes are localized areas of proliferation of the capillary endothelium in the nerve-fiber layer of the retina. Later the nerve-fiber layer is thickened by glial, capillary, and fibrous proliferation which extends into the vitreous, producing a picture resembling retinitis proliferans. Later the retina detaches, and finally the cicatricial stage of retrolental fibroplasia is reached in premature infants.

Banks Anderson and G. Margolis report the effect of ACTH and cortisone therapy in a case of scleromalacia. The local inflammatory symptoms receded. The essential softening and dissolution of the scleral tissue is not affected. The effects of cortisone on corneal lesions, as reported by W. M. James, J. L. Powers, and R. H. Ripple, are in line with Anderson and Margolis' observations, if the scleral tissue is comparable to the corneal stroma.

Superficial punctate keratitis, according to A. E. Braley and R. A. Alexander is probably a virus disease which may be associated with other diseases. Therapy with cortisone and antibiotics is unsatisfactory.

R. N. Berke describes a simplified Blaskovicz operation for blepharoptosis. The best results are obtained in patients with good levator action and normal superior rectus muscles.

In discussing vitreous opacities, Paul A. Chandler makes a most important statement. The most frequent cause of vitreous hemorrhage is the formation of a hole in the retina

with or without detachment.

F. C. Cordes reports a study of 81 cases of optic atrophy in infancy, childhood, and adolescence. Primary atrophy is present in 43 of the 81 cases. The largest single cause of optic atrophy in this group is hydrocephalus (11 cases), neoplastic disease (10 cases). Congenital syphilis is third.

Ludwig von Sallmann and Carmen M. Munoz find intravenously administered cysteine has a markedly protective action against radiation damage to the lens and hair follicles of rabbits.

W. F. Duggan finds the study of color fields to be of value in determining whether a lesion originates in the choroid or in the retina. In five cases of tumor of the choroid the field defect was larger for a blue than for a red stimulus.

The changes in the eye and orbit following carotid legation as observed by Kenneth C. Swan and John Raaf are (1) relief of diplopia and bruit, (2) improvement in the exophthalmos, and (3) the development of a slight cyanosis of the retina with edema and cotton-wool spots. The cyanosis, edema, and cotton-wool spots cleared.

According to A. M. Culler, the intraocular complications of leukemia are produced by anemia which produces hemorrhage and arterial and venous occlusion which produces other lesions. Thrombocytopenia is the most likely cause of terminal hemorrhage in the fundus.

The theses published are: "The ocular aspects of mycotic infection," by Henry L. Birge; "The use of the Sanborn electromanometer in the study of pharmacological effects upon the intraocular pressure," by DuPont Guerry, III; "An experimental study of the evaluation of Hydrosulphosol in the treatment of ocular injuries due to chemical burns," by Robison D. Harley; "The relationship of lenticular changes to mongolism," by Joseph Igersheimer; "Autonomic drugs and their influence on the choroidal vessel caliber," by Irving H. Leopold; "Early wounds in and about the orbit," by Byron Smith.

The contributors to this volume are to be congratulated on their continued curiosity, energy, and enthusiasm.

William M. James.

OCULAR SURGERY. By H. Arruga, M.D. Translated from the third Spanish edition by Michael J. Hogan, M.D., and Luis E. Chaparro, M.D. New York, McGraw-Hill Book Co. Inc., 1952. 936 pages with 1293 illustrations, 127 in color. Price: $36.00.

In the preface to the first edition, the author states that he has followed the rule of describing, along with the techniques that he considers most advantageous, those practiced by the leading personalities in the world of ophthalmic surgery. In the third edition, he has added new techniques and interesting modifications of the old ones. Some original procedures are retained, he says, so that the beginners in ophthalmic surgery may be familiar with the origin of various techniques.

The wide knowledge of ophthalmic literature of all lands possessed by Arruga is attested by the author's index of nearly 600 names, with references in the text to the writings of most of them.

His vast experience and surgical skill are evident in the clarity and adequacy of text, describing without laborious detail the essentials of each operation.

The illustrations are mostly semidiagrammatic, half-tone drawings "highly practical and didactic." They are of sufficient size and accurate detail to enable anyone experienced in ophthalmic surgery to perform the indicated procedures with confidence. Both the artist, Mr. Alemany, and the printers, Imprenta Hispano-Americana, S.A., of Barcelona, are to be commended most heartily on the excellence of this feature. The author has properly provided such visual instruction so generously that most of the described opera-

tive techniques are also pictorially demonstrated.

The chapter on the "Generalities of ophthalmic surgery" contains some excellent suggestions as to the qualifications and conduct of the surgeon. One unusual but excellent bit of advice is that the nervous surgeon may do well to take a mild sedative, such as a short-acting barbituate, one-half hour before operating, to attain calmness and avoid tremor.

The furnishings of the operating room, the illustrated instruments and dressings differ somewhat from those in use generally in the United States but provide a pattern worthy of study by anyone contemplating setting up or improving the surgical workshop, tools, and modus operandi.

The section on "Surgery of the eyelids" fills 149 pages with well-illustrated exposition of operations for all the ordinary conditions as chalazion, entropion, ectropion, epicanthus, and so forth. Different methods are presented enabling the surgeon to refresh his memory on the standard procedure that best suits the problem at hand. Likewise many plastic techniques are presented such as the sliding grafts, pedicle flaps, restoration of the canthus, repair of colobomas, and many others. Here the illustrations enable one to visualize the procedure better than any number of words could do. The techniques for the relief of palpebral ptosis include the classic methods of Elschnig, Blaskovicz, Motais, and others, and some of the later procedures, as the modifications of Berke and the Friedenwald-Guyton suture.

Th "Surgery of the lacrimal apparatus" deals not only with the methods of treating obstruction of the drainage channels but with less common ways of dealing with everted or deformed puncta, absence of tear sac, and so forth. Surgery of the lacrimal gland is treated briefly.

Thirty-five pages are devoted to "Surgery of the conjunctiva" including numerous operations for pterygium, methods of covering the cornea with conjunctival flaps, and the repair of symblepharon.

The "Surgery of the cornea" presents many of the more unusual techniques of keratoplasty as well as those approved by the author. Of considerable interest is the discussion of the technique of tattooing of corneal scars, including the use of colors.

The "Surgery of the iris" describes a surprising number of things that may need to be done to the iris usually as part of the treatment of other conditions.

The treatise on the "Surgery of the lens" is especially full and covers every phase of that most interesting of all problems of ophthalmic surgery, the cataract extraction. The classic operation with full Graefe section, including a narrow strip of limbal conjunctiva, peripheral iridectomy or two iridotomies (Arruga), intracapsular delivery with forceps and hook is described. Following this, a great many of the better known and most useful variations of each of the operative steps are given. The use of preplaced corneal or corneoscleral sutures is mentioned but not stressed. The McLean suture, most popular in America, is not mentioned. The statement is made that iris prolapse occurs in two or three percent of cases even when sutures are used.

Other types of cataract extraction, extracapsular, linear, loop extraction of luxated lenses, even reclination and Ridley's inclusion of a plastic lenticulus are described or mentioned.

The discussions of preliminary preparation of the patient, the postoperative care, and the management of complications are full and practical.

Treatment of retinal detachment is comprehensive and understandable. Much of the material appeared earlier in Arruga's book on this subject. The techniques of treating the region of the retinal tear are generally those adopted by most American authors. The lucid description and illustrations make it possible for the beginner to obtain a men-

tal picture of the procedure which is to be followed.

The section on the "Surgery of glaucoma" devotes little space to the etiologic factors of the various types of glaucoma. The classic operations and many variations in technique are clearly presented by description, illustration, and diagram. The complications and difficulties of each type of procedure are succinctly discussed.

The chapter on "Surgery of the muscles" devotes considerable space to the theoretic considerations which determine the choice of muscle to be operated and what is to be done to it. Then the techniques for producing the desired effects are described. The recommendations of many leading figures in the field of muscle surgery are given along with a great variety of methods of modifying the actions of the ocular muscles.

The final 70 pages of text are devoted to the "Surgery of the eyeball," the vitreous, the orbit, and finally an essay on the subject of intraocular foreign bodies. In this section, as in all the rest, the later developments are mentioned and many of them described in detail. The electronic metal locator could be more fully treated.

As stated in the translator's preface, "The vast experience and surgical skill of Doctor Arruga and the unusual quality of the illustrations make this book a notable addition to the books already available on the subject." The book is recommended to everyone who aspires to do ophthalmic surgery, or teach it, and who needs at times a source where correct techniques and indications for operative procedures can be readily and understandably reviewed.

B. Y. Alvis.

OPHTHALMIC MINIATURE

The Operation for Cataract

A proper cure begins with a purgative, using my Jerusalem pills, compounded only by me. The formula of these is spurge, half an ounce, hepatic aloes, five ounces, to be ground with sugar of roses. After purgation, at the third hour, the patient should be placed astraddle a bench, as if on horseback. Now be seated on the same bench face to face with the patient, who will keep one eye closed. So begins the operation in the name of our Saviour Jesus Christ.

With one hand raise the upper lid, and with the other hold a silver needle and direct it toward the outer lacrimal region. Then perforate the eye coats, pushing and turning the instrument around with the fingers until you touch the diseased matter, which the Saracens and Arabs call *linzaret* (but which we call cataract), with the point of the needle and dislodge it from its position in front of the pupil. Then push it well below, holding it there until you have said four *pater nosters*. Then carefully and slowly turn the needle back to its first position in front of the eye. If the cataract follows the instrument and shows itself in front, you must again depress it, pushing it this time as much as possible toward the ear. Then withdraw the needle in the same manner that it was inserted. And note well that having entered the instrument you must not withdraw it until you are convinced that you have depressed the cataract in the manner just described.

After the operation the patient's eye must be closed, and he should be kept in bed on his back in a shady part of the house. He must not be moved nor allowed to look at a light for eight days, during which period the eye operated on must be dressed with white of egg twice a day and twice during the night. His diet should be soft, fresh eggs with bread. If the patient is young, let him drink water; if old, he may drink a little wine well diluted with water. Many (physicians) allow such patients the meat of chicken, but I prohibit it as being too heavy. That sort of diet causes a rush of blood to the eyes and interferes with natural healing. Finally, after eight or nine days, let the patient make the sign of the Cross and leave his bed. He may now bathe in cold water and so accustom himself to that practice.

Benevenutus Grassus of Jerusalem,
De Oculis Eorumque Egritudinibus et Curis,
Translated by Casey A. Wood, 1929

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Barraquer Cerero, Tomas. **Investigations on the dilator of the pupil.** Arch. Soc. oftal. hispano-am. **12**:507-515, May, 1952.

A histological study of the iris of the catfish demonstrates conclusively the smooth muscle fibers of the dilator of the iris. (7 microphotographs)

Ray K. Daily.

Grawitz, P. B. **The transformation of corneal epithelial cells into cells resembling leucocytes.** Arch. f. Ophth. **152**:312-318, 1951.

More than 300 experiments in rabbits were performed and a central keratitis was produced. The changes of the corneal epithelium were followed for 3 to 24 hours. The normal epithelial cells showed nuclei with a basophilic membrane and an acidophilic center or nuclei containing darker stained nucleoli. After the production of the corneal damage the chromatine of the epithelial cells became rearranged into smaller nuclei. Somewhat later cells resembling leucocytes were formed. This development could be followed step by step. Even where the corneal epithelium appeared to be extremely rich in leucocytes it showed no swelling or increase in volume, as would be expected if the leucocytic elements had entered the central corneal focus from the circulating blood of the corneal periphery. The author feels that his experiments prove the transformation of epithelial cells into leucoytes.

Ernst Schmerl.

Grignolo, A. **Fibrous components of the vitreous body.** A.M.A. Arch. Ophth. **47**: 760-774, June, 1952.

Studies were made of fresh human and bovine vitreous with the phase-contrast microscope designed for the study of transparent material of low contrast. Fibrous elements were observed in fresh preparations which split into progressively smaller elements which anastomosed to form a fairly extensive network posterior to the equator. In human vitreous the network is connected anteriorly with fibrous bundles firmly attached to the vitreous base. The vitreous body is limited by a surface membrane. Studies with the electron microscope showed three types of fibrils, the first with characteristics of collagen; the second a

collagen-like substance; and the third, the most abundant, an unidentified material.

George S. Tyner.

Llorca Rodrigo, J. P. **The cyclopic eye of a human embryo 22 mm. in size.** Arch. Soc. oftal. hispano-am. **12**:184-192, Feb., 1952.

This is a report of a microscopic study of a human embryo 22 mm. long, corresponding to 42 or 44 days of embryonal age. The author believes that this is the third case thus studied and described in the literature, the first two having been reported by Mall. The description is based on 125 microscopic sections and a reconstruction in plastic, enlarged 100 times. This incompletely cyclopic, centrally situated eye contained partially fused elements of both eyes; only the optic fasciculus and the posterior portion of the choroidal fissure were single. The sclera and orbit were single, and the size of the eye suggested a fusion of two eyes. The eye also had an open choroidal fissure, which is abnormal for an embryo of this age, and indicates an arrested development, with resulting coloboma. The other pathologic feature was a great quantity of dense mesenchymal tissue which filled the optic cups and communicated with the extraocular mesenchyme through the choroidal fissure. (7 figures)

Ray K. Daily.

Lopez Marin, I. **The development of the retro-ocular vasculo-nervous system.** Arch. Soc. oftal. hispano-am. **12**:367-385, April, 1952.

The development of the mesenchymal tissue of the orbit in a fetus at birth and human embryos 40, 20, 14 and 10 millimeters in length, is described.

Ray K. Daily.

Poos, Fr. **The oncotic blood pressure as a "Determination Factor" in the development of the normal proportions within the oculo-orbital system.** Arch. f. Ophth. **152**:300-311, 1951.

These theoretical considerations do not easily permit a short abstract.

Ernst Schmerl.

Sautter, H., and Seitz, R. **Studies of the blood supply of the area of the lamina cribrosa in rabbits by retinal and ciliary vessels.** Arch. f. Ophth. **152**:413-424, 1952.

Intravenous injections of trypan blue were administered to living and killed animals, and the anatomical findings are described. The area of the lamina cribrosa is supplied by the central retinal artery. A communication exists between the central artery and the circulus arteriosus sclerae which receives its blood from the short posterior ciliary arteries and the central retinal artery. The flow within the circulus is said to produce suction and to prevent congestion in this area. Arterial connections with the choroid and pial blood vessels supplement this mechanism. Glomus cells were found in the walls of the smaller blood vessels which joined the circulus arteriosus sclerae. These cells were markedly affected by sympathetic-olytic drugs which seem to play a role in the regulation of the blood flow of this area.

Ernst Schmerl.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Tsuchiya, Gaku. **Histochemical study of trachoma inclusions.** Acta Soc. Ophth. Japan **56**:702-705, Aug., 1952.

After treatment with ninhydrin, scrapings from trachoma cases were stained with Schiff's reagent. Inclusion bodies stained rose. The author considers this to suggest the presence of alpha-amino-acid in inclusions. He further studied phosphatase in inclusions by means of chemical techniques and notes that inclusions are positive for alkaline mono- and di-phosphatase.

Yukihiko Mitsui.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Akiya, Hiroshi. **Histochemical study of oxydase and succinic dehydrogenase in the retina.** Acta Soc. Ophth. Japan **56**:764-779, Aug., 1952.

After a freezing dehydration, sections were made from the eyeball of such animals as frog, mouse, rat and rabbit. Cytochrome oxydase and succinic dehydrogenase were analysed in the section by means of histochemical procedures. Both of the enzymes were found in abundance in the layer of rods and cones, in the outer part in particular. In view of the fact that these enzymes are found in mitochondria exclusively, the author concluded that the outer part of the visual cell layer, the spiral, consists of a mitochondrialike substance. His experiment further indicated that, contrary to the general belief, no difference in the amount of oxydase was observed between light and dark-adapted eyes. Yukihiko Mitsui.

Boeck, J., and Klingenberg, H. **The action of pyrazolon derivatives upon the fluorescence of stains.** Arch. f. Ophth. **152**: 514-520, 1952.

The authors studied in vitro and in vivo the action of pyrazolon derivatives upon the fluorescence of fluoresceine. They found that addition of pyrazolon derivatives to the serum does not interfere with the uptake of fluoresceine by the serum colloids. However, the fluorescence of the rabbit's aqueous became markedly diminished. Ernst Schmerl.

Bornschein, H., and Zwiauer, A. **The electroretinogram of the rabbit during experimentally increased intraocular pressure.** Arch. f. Ophth. **152**:527-531, 1952.

The authors studied the retinal activity in rabbits by taking electroretinograms. They found a prolonged latent period and reduction of the b wave when the intraocular pressure was increased to 50 or 70 mm. Hg. The electroretinogram completely disappeared when the pressure reached 90 mm. Hg. This finding is in agreement with former studies where at the same pressure a delayed discoloration of the injected and stained blood vessels of the choroid had been observed.

Ernst Schmerl.

Boros, B., and Takats, I. **Cannon's law of denervation and the problem of the double innervation of the iris.** Arch. f. Ophth. **152**:319-334, 1952.

Cannon and Rosenblüth found that organs become oversensitive to the chemical transmitters of nervous stimulation after they are denervated. With this law in mind the authors studied the question whether the sphincter iridis has a sympathetic innervation. They removed the cervical sympathetic of one side in 32 cats and demonstrated the increased sensitivity to adrenaline in the isolated sphincter preparation. Controls using tissues of the normal sides of the animals were negative. The parasympathetic innervation of the sphincter iridis is known. These experiments therefore support the theory of the double innervation of this muscle.

Ernst Schmerl.

Cannon, E. J., and Leopold, I. H. **Effectiveness of terramycin and other antibiotics against experimental bacterial keratitis.** A.M.A. Arch. Ophth. **47**:426-436, April, 1952.

This study is a comparison of the effectiveness of terramycin, neomycin, chloromycetin, aureomycin and streptomycin against standard pure culture corneal infections of the rabbit eye. Despite the antibiotic used, the prognosis of the inoculated eye was definitely poorer unless the treatment was instituted within one hour. Terramycin proved effective in a variety of infections with Gram-positive,

penicillin-resistant, and Gram-negative organisms. Neomycin apparently was the next most effective drug used. (6 figures, 10 references) George S. Tyner.

Caselli, F., **Action of vitamin E on the blood-aqueous barrier.** Boll. d'ocul. **31**: 271-280, May, 1952.

Six rabbits were given hydrosoluble vitamin E_t 60 mg. per kg. body weight, intravenously, for 10 days. The fluorescein curves were determined according to Huber and Amsler at varying intervals, between two and nine hours after the vitamin administration. The permeability of the iridociliary capillaries was found to be reduced in all experiments. (1 figure, 2 tables, 21 references) K. W. Ascher.

Corrado, M. **Stimulation of the trigeminal nerve and its relation to chemical mediators.** Arq. portug. de oftal. **3**:63-72, 1952.

The author made a quantitative determination of the histamine content of the aqueous humor of a dog by the direct biological method of Barsoum and Gaddum. Histamine was absent in those eyes in which the first division (ophthalmic) of the trigeminal nerve had been sectioned, and the peripheral stump stimulated electrically. The histamine content of the opposite, intact eye was normal. This observation may be explained by an inhibitory action of albumin which appears in large quantity as a result of increased vascular permeability of the stimulated eye. Corrado compares his findings with those of authors who have investigated other sensory nerves. James W. Brennan.

Dorello, Ugo. **Glutathione in the crystalline lens.** Rassenga ital. d'ottal. **21**:172-184, May-June, 1952.

The percentual content of glutathione is much greater in the crystalline lens than in any other structure of the body and greater than in any other portion of the eye. However, the percentage given by different observers varies considerably. Dorello found a decrease in the content of glutathione percentage of rabbits' lenses after the administration of ACTH and DCA parenterally. Such a decrease may be hypothetically attributed to the action of the DCA, perhaps through a mechanism of "stress." (Note: I do not know what DCA is—only the initials are used through the article.) Eugene M. Blake.

Dorello, Ugo. **The local action of tetraethylammomium phosphate (TEA).** Rassegna ital. d'ottal. **21**:96-101, March-April, 1952.

Having previously experimented upon rabbits by the subconjunctival injection of TEA the author extended his observations upon human eyes. The doses employed were 0.10 mg., 0.50 mg., and 1 mg. Repeated tests were made upon 12 subjects with noninflamed eyes. After the injection, 1-percent atropine, 2-percent pilocarpine and one-half-percent eserine were instilled into the conjunctival sac. It was found that considerably larger doses were required to be effective in man. The experiment proved that TEA blocks the postganglionic fibers and the ganglion synapses made inactive to the receptors sensitive to acetylcholine. The action is similar to that of curare.

Eugene M. Blake.

Dorello, U., Calamandrei, C., and Montanari, L. **The action in vitro of sodium propionate on some of the commoner pathogenic bacteria affecting the eyes.** Ann. di ottal. e clin. ocul. **78**:137-146, Feb., 1952.

The authors found that sodium propionate in a concentration of 5 percent or less inhibits the growth of all 13 of the common bacteria with which they experimented in vitro. Its bacteriostatic effect on Moraxella lacunata, Moraxella liquefaciens, Haemophilus influenzae, and

Haemophilus pertussis has not, according to the authors, been previously reported. (References) Harry K. Messenger.

Dorello, U., Calamandrei, G., and Montanari, L. **In-vitro action of some antibiotics and antiseptics on less common pathogenic organisms.** Boll. d'ocul. **31**: 281-290, May, 1952.

The authors studied the in-vitro action of sodium propionate, penicillin, terramycin, streptomycin, chloromycetin, aureomycin, bacitracin, sulfacetimide, protargol, argyrol, zinc sulfate, and methylene blue on Escherichia coli, Bacillus enteritidis, Bacillus subtilis, Staphylococcus aureus, Staphylococcus albus, Streptococcus hemolyticus, Streptococcus viridans, Diplococcus pneumoniae, Klebsiella pneumoniae, Moraxella lacunata, Moracella liquefaciens, Hemophilus influenzae, and Hemophilus pertussis. Growth inhibition was found when penicillin, streptomycin, chloromycetin, aureomycin, terramycin, bacitracin, sodium propionate were used; methylene blue had no inhibiting effect while sulfacetimide, protargol, argyrol, zinc sulfate inhibited some of these germs only. (18 references) K. W. Ascher.

Ely, L. O. **The cytochrome-C content of bovine crystalline lens.** A.M.A. Arch. Ophth. **47**:717-719, June, 1952.

Quantitative spectrophotometric analysis indicates that there is on the average 2.53γ of cytochrome C per bovine lens. Isolation of cytochrome C in the lens supports the assumption that there is a citric-acid cycle in the lens metabolism. The method of determination is described; 200 lenses were used. George S. Tyner.

Kleinert, Heinz. **The visible venous flow of the aqueous.** Arch. f. Ophth. **152**:278-299, 1951.

The well known phenomenon of the granular flow of the blood in epibulbar veins, in pericorneal and in deep corneal vessels is demonstrated by a number of pictures. The author feels that these observations present an adequate basis to explain this phenomenon as an aqueous backflow in these vessels due to osmotic forces. Ernst Schmerl.

Meesmann, A. **Experimental studies of the double innervation of the ciliary muscle.** Arch. f. Ophth. **152**:335-356, 1952.

The author studied the ciliary muscle of freshly enucleated and fenestrated eyes of rabbits, cows, pigs, dogs and cats. Cinematographically obtained curves show the action of drugs and faradic stimulation upon the ciliary muscle. Acetylcholine and pilocarpine produced an extreme contraction, glaucosan and adrenaline a stretching of the muscle fibers. The response to faradic stimulation became inhibited by each of the drugs. The experiments support the theory of the double innervation of the ciliary muscle. Ernst Schmerl.

Michaelson, I. C. **Effect of cortisone upon corneal vascularization produced experimentally.** A.M.A. Arch. Ophth. **47**: 459-464, April, 1952.

The effect of subconjunctival cortisone upon the formation of corneal vessels after production of corneal lesions in rabbit eyes with a platinum-wire cautery was studied. The author successfully produced similar bilateral lesions in 18 rabbits. Cortisone reduced the extent of vascularization by about 45 percent and the rate of longitudinal growth by about 30 percent. The effectiveness of the cortisone was proportional to the distance of the lesion from the limbus. The technical difficulties of standard procedure in such a study seem obvious. (1 figure)

George S. Tyner.

Mueller, H., and Maumenee, A. E. **Experimental transplantation of sclera**

into the cornea. Arch. f. Ophth. **152**:521-526, 1952.

Thirty-one scleral transplants in rabbits did not become transparent.

Ernst Schmerl.

Pau, Hans. **Experimentally produced lens opacities.** Arch. f. Ophth. **152**:532-538, 1952.

The author tries to demonstrate that neither the inhibition of the metabolism of the lens nor the maintenance of the normal ratio between sodium and potassium is linked to the transparency of the lens. Opacities are said to be caused by an uptake of fluid and structural changes of the proteins. Ernst Schmerl.

Pau, Hans. **The compensation test, an in vitro arrangement to retain the normal weight and transparancy of the lens.** Arch. f. Ophth. **152**:539-544, 1952.

If lenses are placed into solutions which exercise a normal osmotic pressure and an oncotic pressure of about 1000 mm. H_2O, they retain their weight and transparency for more than 20 hours. The author used for his experiments Kollidon 90 which is manufactured by I. G. Farben.

Ernst Schmerl.

Siliato, Francesco. **Experimental study of the mucolytic action in vivo of hyaluronidase in the cornea.** Ann. di ottal. e clin. ocul. **78**:241-250, April, 1952.

Siliato reports his experiments whereby he found that hyaluronidase, when injected into the cornea of rabbits, has a mucolytic action in vivo, depolymerizing and hydrolyzing the hyaluronic acid of the cornea, as shown by the liberation of glucosamine. Further study of the action of this enzyme system in the cornea may lead to a reinterpretation of certain keratopathies in the light of our newly acquired knowledge of collagen diseases. (References) Harry K. Messenger.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Brock, F. W., and Givner, I. **Fixation anomalies in amblyopia.** A.M.A. Arch. Ophth. **47**:775-786, June, 1952.

A new test, which is a modification of the after-image test, is described for measurement of fixation disparities. It differs from others in that only one eye is exposed to the filament which the latter is in a vertical position. The good eye is stimulated while the amblyopic eye is totally occluded. After two exposures on the same eye the occluder is moved to the good eye and the patient attempts to maintain fixation on a test chart with his amblyopic eye. The appearance of the after image of the exposed eye with relation to the fixation object is significant. If the after-image is centered on the fixation object, fixation ability of both eyes is said to exist. Eccentric fixation is indicated if the after-image is not centered on the fixation object. It was found that 1. about 20 percent of persons with uniocular amblyopia fixate along the central-foveal axis of the poor eye on occlusion of the good eye; 2. most people with uniocular amblyopia fix eccentrically, the greater the amblyopia the greater the eccentricity; 3. 80 percent of cases of alternating strabismus are incapable of after-image transfer, 75 percent of people with unilateral strabismus show transfer ability; and 4. the acuity gradient in amblyopia shows a small central depression or total loss of vision not explained by "obligatory cortical inhibition."

George S. Tyner.

Clark, Ivor G. **Important implications of the plus three error of refraction.** Ohio State M.J. **48**:601-602, July, 1952.

The author reviews the symptoms that may occur in the patient with a plus three error of refraction, not excluding astig-

matism, namely, stomach distress, dizziness and sensation of blacking out. It is also pointed out that the eye itself may suffer from belated care. The globe is too small and the constant incessant activity of the ciliary mechanisms necessitated by excessive hyperopia, increases the bulk of the ciliary muscle producing a shallow anterior chamber, thereby blocking off the canal of Schlemm and creating ideal conditions for development of glaucoma. The results to be anticipated by careful study of this group of patients are 1. greater comfort for head, eyes and eyelids, 2. better and easier vision, 3. fewer ocular lesions, and 4. less blindness.

Morton Cutler.

Contardo, R. **Tinted lenses in ophthalmology.** Arch. chil. de oftal. **22-23**:69-78, Dec., 1949.

The majority of tinted lenses are not prescribed by ophthalmologists, and have no actual protective value against harmful radiations. The normal eye does not require such filters, except in a few areas where the sun is especially bright, or where reflection produces a dazzling sensation. However, certain eyes, notably with albinism, aphakia, iritis, and keratitis are abnormally sensitive to light and in certain occupations such as welding and working in glass or metal there is exposure to ultraviolet or infrared radiation. One investigator, Zaretskaya, reported a reduction in intraocular tension when the eye was exposed to green light. The mode of action is obscure, and may involve alteration of the vegetative nervous system. In aphakia, the absence of the crystalline lens may produce erythropsia, as the normal lens acts as a filter of certain wave lengths near the violet end of the spectrum. A tint may add to the patient's comfort and, in addition, avoid possible retinal damage from ultraviolet and infrared radiation.

In general, the filters act by absorption and reflection of the harmful wave lengths, and by reduction of the intensity of the rays which are transmitted. They are made by combining glass with substances which have absorbent properites such as gold, copper, iron, manganese, cobalt and chromium. In addition, a polarizing lens is available which is of value in eliminating rays of light reflected, for example, by water. They contain a pellicle of submicroscopic crystals oriented in the same direction. They have the disadvantage of producing peripheral distortion.

The author feels that in the average patient tinted lenses are unnecessary. In those instances where protection is necessary, absorption and reflection of ultraviolet and infrared radiations are possible with many types of colored lenses. Several graphs are presented to show transmission of various wave lengths.

James W. Brennan.

Cüppers, C., and Wagner, E. **The influence of drugs on the retinal function.** Klin. Monatsbl. f. Augenh. **118**:288-308, 1951.

This is the second of a series of articles by the authors. It deals with the influence on normal cone function and with the therapy of impaired dark adaptation. They used Helenien (Adaptinol), a lutein found by v. Studnitz in the lipoid-droplets of cones. In addition, a water-miscible form of vitamin A was used. Contrary to the findings of v. Studnitz and others, the authors did not find an influence on color vision by the administration of Adaptinol. Both drugs improved the dark adaptation, provided the lesion was not organic.

Frederick C. Blodi.

Heinsius, E., and Grevsmühl, G. **Diagnosis of the various types of colorblindness with the colored dots of Trendelenburg.** Klin. Monatsbl. f. Augenh. **118**:269-282, 1951.

The authors re-examined the color test

with dots designed by Trendelenburg and improved by Ahlenstiel. Contrary to the first claims, this test, in the hand of the authors, did not allow the differentiation of protanopes from deuteranopes, nor the separation of the deuteranomalous and the protanomalous from normal trichromates. The test also requires a high degree of intelligence.

Frederick C. Blodi.

Jaeger, W. **Congenital total colorblindness with traces of color vision.** Klin. Monatsbl. f. Augenh. **118**:282-288, 1951.

A 49-year-old patient with all the classical symptoms of congenital total colorblindness showed some color vision when the visual angle was larger than 12°. While the vision was monochromatic for a smaller field, defective dichromatic vision existed for larger objects. The luminosity curves corresponded to these findings. The heredity was a simple recessive one. Frederick C. Blodi.

Monjé, Manfred. **Pharmacodynamic and clinical studies of the accommodation.** Arch. f. Ophth. **152**:357-378, 1952.

The author studied the accommodation in men using adrenaline and homatropine in patients with unilateral paralysis of the sympathetic (Horner's syndrome). Adrenaline was found to increase the distance of the nearpoint in eyes with motor paralysis produced by homatropine. Adrenaline itself had the same effect for a shorter period of time. In patients with Horner's syndrome the distance of the nearpoint was found to be diminished.

Ernst Schmerl.

Morgan, M. W. **Relationship between accommodation and convergence.** A.M.A Arch. Ophth. **47**:745-759, June, 1952.

This is a review of the literature and a discussion of the relationship between accommodation and convergence. The author believes that convergence is a complex function which can be divided into the elements of tonic convergence, accommodative convergence, relative fusional convergence and proximal convergence. He believes that accommodative convergence is extremely stable in any one subject and bears a linear relationship to accommodation. There is true relative convergence but no relative accommodation. Binocular vision with changes in ametropia and correction lenses is made possible not by a dissociation of the functions of accommodation and convergence, but by a variation in relative convergence.

George S. Tyner.

Ogle, K. N. **Optics and visual physiology.** A.M.A. Arch. Ophth. **47**:801-830, June, 1952.

This is a complete review of the year's literature. (155 references)

George S. Tyner.

Piper, Hans-Felix. **The sensory and motor function of the eye.** Arch. f. Ophth. **152**:425-476, 1952.

The author uses the principle of color haploscopy to study spatial perception in man and arrives at the conclusion that spatial perception depends upon a series of correlated and more or less differentiated sensory and motor functions. The original paper must be consulted for technical details. Ernst Schmerl.

Priklonsky, M. **The best illumination when testing color vision with pseudo-isochromatic tables.** Klin. Monatsbl. f. Augenh. **118**:259-269, 1951.

The author emphasizes the importance of daylight or an equivalent artificial illumination for the testing of color vision with pigments. Frederick C. Blodi.

Richter, M. **Some newer theories of color vision.** Klin. Monatsbl. f. Augenh. **118**:240-259, 1951.

The author gives a survey of some of

the modern trends in the theory of color vision. Most of the recently found factors (Studnitz, Granit) favor the trichromatic theory. Frederick C. Blodi.

V. Studnitz, G. **The color vision of vertebrates.** Klin. Monatsbl. f. Augenh. **118**: 225-240, 1951.

This is the second article of a series prepared for ophthalmologists by the distinguished German physiologist. He first reviews the results of Stiles and Crawford who obtained three peaks in the luminosity curve of the photopic eye and so found another proof for the trichromatic theory of color vision and for the existence of three different types of cones. Other factors in favor of the trichromatic theory are the modulator curves found by Granit in isolated nerve-fibers in various vertebrates. Granit believes that there are only three types of modulator curves which could be the retinal equivalents of the three basic color perceptions. Studnitz warns not to correlate too closely electrophysiologic phenomena of optic nerve fibers with the bleaching of visual substances by light. He denies the existence of a receptor for red. Other proofs of this theory are the results of experiments (Tonner, Loevenich) testing visual acuity with monochromatic light. The acuity is poorer if a light is used which incites only one type of cone. It is better with a light stimulating two or all three types.

Studnitz had maintained that three different types of lipoid-droplets are present in the cones. This proved to be true by chemical analysis. The visual substance of yellow-green contains as a chromophoric group a carotenoid (lutein, helenien) which when administered orally, improves dark adaptation. Frederick C. Blodi.

Yamagishi, Rikuo. **A clinical use of flicker test.** Acta Soc. Ophth. Japan **56**: 820-832, Aug., 1952.

The author compared the critical frequency in a flicker test and the visual acuity. The critical frequency was not influenced by the error of refraction. Then he measured the critical frequency in eyes which had artificially been made heteropic by giving various lenses in atropinized emmetropic eyes; thus he found an inalterability of the critical frequency by the change of refraction. Finally he concluded that a flicker test gives an indication of an essential sensitivity of the retina and, therefore, the test should be used widely in routine clinical examination along with tests of visual acuity. He further studied such factors as the intensity of illumination and the size of the light disc, which cause a change in the critical frequency. Yukihiko Mitsui.

5

DIAGNOSIS AND THERAPY

Arentsen, J. **Ocular tuberculosis treated with streptomycin: biomicroscopic control.** Arch. chil. de oftal. **22-23**:107-108, 1949.

These are conclusions arrived at during a joint meeting of ophthalmologists and tuberculosis investigators. Streptomycin is bacteriostatic, not bactericidal. Treatment must be prolonged so that the invading organism may be destroyed or eliminated. The bacteriostatic action begins as soon as the drug comes in contact with the bacillus. Exudates and exudative processes disappear completely in weeks or months without leaving any trace. When the tubercles, which are destructive processes, heal, they leave scar tissue which may be more extensive than the original lesion. Should this occur in specialized tissue, the function of the tissue is partially or completely lost. Cicatricial tissue is preceded by the formation of new blood vessels which invade the avascular tubercles. Keratic precipitates become smaller and the edges stellate, with pigmentation on the posterior surface. They

may take six months to disappear. Cells do not disappear from the aqueous until these precipitates are gone. Nodules of the iris border may form dense synechiae with resultant secondary glaucoma. Destruction of the organism is by means of tissue defenses, as the drug only retards action of the bacillus. Healing is more rapid in small lesions, hence the necessity of early and accurate diagnosis.

James W. Brennan.

Arruga, H. **Experience with cortisone in ophthalmology.** Arch. Soc. oftal. hispano-am. **12**:123-127, Feb., 1952.

Arruga confirms the report of favorable results achieved with the use of ACTH and cortisone in inflammatory conditions of the anterior ocular segment. The only complication he encountered was a white, bright infiltration, occupying the center of the cornea in a case of herpetic keratitis, which appeared after six subconjunctival injections of cortisone and three daily instillations. The infiltration disappeared 20 days after the medication was discontinued. A serous macular retinopathy which failed to improve with instillations and subconjunctival injections of cortisone improved significantly on the internal administration of cortisone tablets. A case of sympathetic ophthalmia which was not influenced by instillations and subconjunctival injections of cortisone improved on injection of ACTH. (2 figures)

Ray K. Daily.

Bartolozzi, R. **The problem of headaches in ophthalmology.** Arch. Soc. oftal. hispano-am. **12**:411-430, April, 1952.

The literature is reviewed.

Ray K. Daily.

Belmonte Gonzalez, Nicolas. **Binocular ophthalmoscopy with Goldman's contact lens of the periphery of the fundus in the study of retinal detachment.** Arch. Soc. oftal. hispano-am. **12**:386-390. April, 1952.

The author advocates systematic examination of the fundus with the slitlamp and Goldman contact lens. Using the different mirrors of this lens one can explore two different regions of the retina; the region between the equator and the ora serrata, and that of the posterior pole. The study of the fundus in this manner is more rapid, easier, and more reliable, for the bright light of the slitlamp penetrates cloudy media better than the light from the ophthalmoscope, and binocular vision permits of easier differentiation between a small hemorrhage and a tear. Ray K. Daily.

Berens, Conrad. **Plastic compressor for enucleation and evisceration.** J.A.M.A. **149**:1316-1317, Aug. 2, 1952.

A lucite® modification of the enucleation compressor devised by Anthony is described. It is U-shaped, with an ovoid compressor tip at each end, one 14 mm. in diameter for adults, and the other 11 mm. in diameter for children. Pressure with the compressor tip controls hemorrhage from the central retinal vessels without the bulk of tampons, and even allows for simultaneous closure of Tenon's capsule. (2 figures, 1 reference)

Harry Horwich.

Boros, B., Méhes, G., and Arató, M. **Biologic properties of the placental extracts (Filatow).** Klin. Monatsbl. f. Augenh. **118**:308-315, 1951.

The authors tested the pharmacological properties of placental extracts prepared according to Filatow. The effects were histamine-like and after subconjunctival injection of these extracts histamine was found in the tissue.

Frederick C. Blodi.

Desvignes, P., Fontaine, M., and Caris, J. **First lessons in the psychosomatic treatment of eye diseases.** Ann. d'ocul. **185**:588-617, July, 1952.

Symptoms such as reduced vision and

pain may be aggravated by adverse emotions, such as the fear of blindness. Similarly, symptoms may be reduced or even temporarily cured by reducing the associated autonomic imbalance by suggestion which increases the urge and the will to recover. In more than 50 percent of 51 selected cases with structural ocular diseases vision was more or less permanently improved by psychosomatic treatments. These treatments were independent of any treatment for any structural disease. Usually three or four treatments were given at weekly intervals and consisted of hypnosis, psychoanalysis and suggestion. The exact details are not described. The literature is reviewed and several illustrative cases are presented. In the first case the corrected vision improved from 0.1 to 0.7 in each eye after psychosomatic treatment. The patient was a 30-year-old woman with high myopia and choreoretinal atrophy. In the second case the corrected vision was improved from 0.2 to 0.5 in each eye after four psychosomatic treatments. The patient was a 25-year-old man with high myopia, floating vitreous opacities, and choreoretinal atrophy. In the last case, vision was materially improved and the inflammatory symptoms decreased after this type of therapy in a patient with amblyopia, blepharitis, and a high refractive error. This contribution is of interest because it emphasizes the frequent discrepancy between the functional and structural evidences of disease and because it explains the method of influencing autonomic imbalance by suggestion. Unfortunately, however, the improvement which follows therapy by suggestion is usually only transient. Chas. A. Bahn.

Dolcet, L. **Ridley's lens and a carborundum mandrill.** Arch. Soc. oftal. hispano-am. **12**:516-517, May, 1952.

The author describes a compact electric drill, for dacryocystorhinostomy, to which may be attached a carborundum mandrill for reducing the size of a Ridley lens, when it seems too large. The apparatus is also useful for making alterations in plastic contact lenses and artificial eyes. (1 figure) Ray K. Daily.

Fine, M. **An improved manually operated erysiphake.** A.M.A. Arch. Ophth. **47**:513-514, April, 1952.

The author describes an improved manually operated erisophake. A fountain-pen principle is applied to the instrument to provide a stronger suction than the ordinary bulb erisophake and less suction than the vacuum pump. (1 figure)

George S. Tyner.

Fine, M., and Goodwin, R. C. **Evaluation of local cortisone therapy in ophthalmology.** A.M.A. Arch. Ophth. **47**:787-797, June, 1952.

Cortisone was used topically and by subconjunctival injection on 121 patients with ocular disease. In a variety of diseases 50 showed a definite therapeutic response, 29 a doubtful or equivocal response and 42 no response. The most favorable response was obtained in cases of marginal corneal ulcer due to bacterial hypersensitivity, disciform keratitis, nonluetic parenchymatous keratitis, allergic conjunctivitis, acute nongranulomatous iritis, sympathetic ophthalmia, postoperative iridocyclitis due to lens debris and endophthalmitis phacoanaphylactica. It is not advisable to use cortisone in acute or chronic pyogenic infections, tuberculous disease, acute virus infections and postoperative conditions in which prompt wound healing is essential.

George S. Tyner.

Franceschetti, A., Sarasin, R., and Blavoine, C. **A few indications for roentgen therapy in ophthalmology.** Am. J. Roentgenol. & Rad. Therapy **68**:38-46, July, 1952.

The value and indication for various forms of roentgen therapy in ophthalmology are discussed. Radium is not included in the authors' plan of therapy because the salt is difficult to use and the harder rays may have a deleterious effect on the lens. The two types of radiation recommended are 1. X-rays of definite wave length or Bucky (grenz) rays (very soft), 2. superficial roentgen therapy. Therapy with grenz rays is considered to have a favorable influence in cases of discoid keratitis resulting from herpes zoster and indolent and refractory ulcers of the cornea. Therapy with roentgen rays is indicated in posttraumatic iridocyclitis, resistant iritis (treatment led to clearing of vitreous floaters), and preoperative radiation of the corneal site in contemplated corneal grafts if there is a tendency to form keloids. The authors also suggest irradiation for relief of symptoms accompanying postoperative bullous keratitis, and this therapy is also used in the treatment of thrombosis of the retinal veins. The schedule of doseage used by the authors is indicated. Stanley D. Golden.

Friede, R. **Therapeutic stasis in diseases of the anterior segment of the eye.** Klin. Monatsbl. f. Augenh. **118**:181-185, 1951.

The author suggests venous hyperemia as a treatment in various inflammatory diseases of the anterior segment. A series of suction-cups for this purpose is presented. Frederick C. Blodi.

Grancini, L. E. **Blindness in young children, from the point of view of its possible treatment.** Ann. di ottal. e clin. ocul. **78**: 121-130, Feb., 1952.

Various forms of blindness are discussed with reference to treatment, which in general should be undertaken as early as possible. For leukomas of the cornea Grancini recommends first making a trial with a contact lens, which is well tolerated in children, then an iridectomy, and keratoplasty as a last resort. His preferred operation for congenial glaucoma is a goniotrabeculotomy. Certain cases of blindness not amenable to surgery have been indubitably benefited by implantations of placental tissue near the eye and by treatment with injections of extracts of cod liver oil and other substances and with cellular lysates.

Harry K. Messenger.

Larmande, A. M. **A thread retractor for the iris.** Ann. d'ocul. **185**:552-557, June, 1952.

The author advocates the use of thread as a retractor of the iris. To put it in place a curved needle is passed through the pupil, behind the iris, and out through the opening made by a preparatory peripheral iridectomy. When the iris is pulled up by means of this thread and the corneal flap down by means of a preplaced suture, the lens is completely exposed. Drawings show details of the operation. (4 figures, 3 references)

B. T. Haessler.

Mariotti, Lorenzo. **Kasakow's polylysate therapy in ophthalmology.** Ann. di ottal. e clin. ocul. **78**:327-334, May, 1952.

Mariotti used Lysuvea, a polylysate of uveal tissue in nine cases of retinitis pigmentosa and 29 of various diseases of choroid and retina. Improvement in the former was prompt but not lasting; more marked and lasting improvement, hardly achievable by other means, was noted in some of the latter, particularly in exudative diseases. The theory of Kasakow's treatment with organ-specific polylysates is discussed. The polylysates are thought to act by increasing the permeability of the cellular membrane and thus to permit a rapid functional recovery by restoring to the protoplasm those substances lost in the exudative process. They have antiexudative, antiphlogistic, and reparative

properties, and may be used with other forms of therapy. (References)

Harry K. Messenger.

Melodia, Corrado. **Local therapy with cortisone in certain ocular affections.** Ann. di ottal. e clin. ocul. **78**:363-374, May, 1952.

Melodia briefly reviews the literature and reports his experience with cortisone ointment ½ to 1 percent five times daily in 57 patients with various diseases. Best results were obtained in allergic blepharitis and conjunctivitis, in nodular and diffuse episcleritis, in syphilitic interstitial, traumatic, bullous, and superficial punctate keratitis, in acute inflammation of the uveal tract, in hypertensive uveitis, and in one case of tuberculous iritis. Results were doubtful in phlyctenular keratitis, in a case each of paramacular choroiditis and of sympathetic ophthalmia, and in the prevention of complications in keratoplasty. The treatment was ineffective in herpetic keratitis and in three cases of Fuchs's epithelial dystrophy. Experience with three Elliot's corneoscleral trephining operations and with four extracapsular cataract extractions suggests that cortisone can be valuable postoperatively when an intense uveal reaction is feared. By its antiallergic and anti-inflammatory action cortisone can reduce tension in hypertensive iritis and can bring about regression of newformed vessels, but in the absence of inflammation it does not retard neovasculogenesis. (References)

Harry K. Messenger.

Morgan, A. L., Crawford, J. S., Pashby, T. J., and Gaby, J. R. **Survey of methods used to reveal eye defects in school children.** Canad. M.A.J. **67**:29-34, July, 1952.

A study of 1,200 children in Toronto public schools was made with various types of eye tests. The Snellen illiterate "E" chart is an adequate test for visual acuity in the kindergarten age. A visual acuity of 20/30 in each eye can be regarded as normal. In grades one to eight a visual acuity of 20/20 in each eye is normal. The Snellen number chart is adequate for testing visual acuity in grade one and the Snellen letter chart for grades two to eight. Adequate illumination of the Snellen chart is necessary and can be about 10 footcandles supplied by a lamp with a reflector on each side of the chart and three feet away with a 100 watt daylight bulb in each. Color vision can be tested adequately by Holmgren wools in kindergarten age and by the pseudo-isochromatic or Ishihara plates in the older children. Tests for phorias were equivocal and the emphasis to be placed on phorias is problematic. Martin Ackerman.

Ohm, J. **Frequency, the most important quality of miners' nystagmus.** Arch. f. Ophth. **152**:477-484, 1952.

From 1914 to 1950 the author studied more than 1,000 cases of miners' nystagmus. During this period the frequency of the nystagmus movements per minute increased by about 30 vibrations, possibly due to the improved illumination of the mines. Ernst Schmerl.

Peruzzo, L., and Rama, G. **General anesthesia in ophthalmology.** Ann. di ottal. e clin. ocul. **78**:279-286, April, 1952.

The authors describe their method of general anesthesia with nitrous oxide, oxygen, and ether, with intubation, and recommend it, as being safe and without serious complications, for ophthalmic operations in young children. (1 figure, references) Harry K. Messenger.

Piper, Hans Felix. **Understanding the fundus changes.** Arch. f. Ophth. **152**:153-200, 1951.

Several generally known fundus pictures are presented for the purpose of classifying the conditions according to localisation, of the changes, course, and relation to general conditions. Ernst Schmerl.

Puglisi-Duranti, G. **Local treatment in eye disease.** Boll. d'ocul. **31**:233-242, April, 1952.

Cortisone was given in drops, ointment, and subconjunctival injections. No improvement was noted in late trachoma; the results were good in early trachoma, episcleritis, follicular conjunctivitis, vernal conjunctivitis, and traumatic uveitis. After cessation of treatment, exacerbations were observed in episcleritis and vernal conjunctivitis. (References)

K. W. Ascher.

Regard, Edouard. **An apparatus for the examination of diplopia in a darkroom.** Ann. d'ocul. **185**:537-542, June, 1952.

Regard has designed a piece of apparatus for schematizing the red glass test for diplopia. It consists essentially of a box in which are six electric light bulbs and the front of which has superimposed a sliding panel provided with slits. By appropriate adjustment of the panels a rectangular area of light can be exposed in various positions such that when viewing them the patient brings his eyes into each of the cardinal directions of gaze. Among the principal advantages are the dimensions (reduced to 80 cm.) which permit it to be used in even a small darkroom, and reduction of the nine lamps of the standard diapositive to six. The author has found it most useful in the six years since its construction. (3 figures) B. T. Haessler.

Remky, Hans. **Disturbances of the regulation of the retinal blood-circulation in diseases of the brain, its vessels, membranes and nerves.** Arch. f. Ophth. **152**: 248-277, 1951.

The retinal bloodpressure is dynamometrically determined with the patient in the upright and in the recumbent position. Certain pressure differences for both positions are considered as normal values and deviations from these differences are called disturbances of regulatory mechanisms due to a hyper- or hypotony of the vascular walls. The author gives as normal findings a change in pressure in the horizontal position up to +9 percent in younger persons, up to +3 percent in middle aged people and up to −5 percent in patients 60 years old and over. He finds deviations from these values (usually a hypertony) in patients with cerebral trauma, with brain tumors, and with damaged cerebral blood vessels. Hypotony combined with a normal papilla is said to be a sign which is diagnostic of the absence of a space-taking intracranial process and hypertony of its presence. Hypertony combined with papilledema might be caused by a blockage of the cerebral cysternas. Ernst Schmerl.

Romero Robles, Eduardo. **An experiment on the mechanism of ocular refraction.** Arch. Soc. oftal. hispano-am. **12**:518-521, May, 1952.

A device, to demonstrate the action of accommodation is described. It demonstrates that the radial fibers of the ciliary muscle flatten the lens and focus it for distance, and act as antagonists of the circular fibers. The contrivance used for this purpose consists of a copper ring, to the anterior third of which is attached a string doubled in the middle; the separated threads represent the surfaces of the lens. Needles are inserted at each end of the thread which are acted upon by a magnet. The movement of the needles produces traction on the threads, which corresponds to the effect of a contraction of the ciliary muscle on the lens surfaces. (5 figures)

Ray K. Daily.

Vesey, F. A. **A new operating phantom for animal-eye surgery.** A.M.A. Arch. Ophth. **47**:798, June, 1952.

A new instrument is described for use in operating on excised eyes for teaching purposes. George S. Tyner.

Woods, A. C., and Wood, R. M. **Studies in experimental ocular tuberculosis.** A.M.A. Arch. Ophth. **47**:477-512, April, 1952.

Extensive experiments were undertaken to determine what effect, if any, continued treatment with the adrenocortical hormones might have on developing ocular tuberculosis in the normal and in the immune-allergic rabbit. The following conclusions were made: 1. Cortisone, Compound F and probably ACTH are contraindicated in ocular tuberculosis. 2. ACTH, cortisone and Compound F do not control either subjective symptoms or the development of organic tuberculous lesions in the eyes of normal, non-immune rabbits. 3. When treatment in normal rabbits is concluded, there is some accentuation of local inflammation and possibly further systemic spread. 4. Cortisone topically or parenterally will block focal reaction to tuberculin and early development of lesions in the immune-allergic rabbit. 5. After 30 to 45 days those agents are no longer capable of blocking either subjective signs or the development of organic lesions. 6. Compound F was less effective than cortisone or ACTH in suppressing the focal reaction to tuberculin, early inflammatory reaction and the development of tuberculous lesions. 7. With termination of treatment with Compound F or cortisone in the immune-allergic rabbits, there is violent increase in the degree of ocular inflammation and local spread of the lesions. (22 figures, 9 references)

George S. Tyner.

6

OCULAR MOTILITY

Carlevaro, G. F. **The prevention and treatment of amblyopia ex anopsia in nursery schools.** Ann. di ottal. e clin. ocul. **78**:147-155, Feb., 1952.

Every nursery school should have a program for detecting and treating amblyopia ex anopsia such as is already in operation in Milan. The good eye should be occluded for at least a month, and meanwhile the vision of the squinting eye should be stimulated with appropriate exercises. Books with large type should be provided. In discussing this paper Foroni remarks that all of us would benefit if printing were in black on a greenish background instead of on white. White produces a certain dazzling and so weakens the retinal image of the print. (A chart of optotypes for children)

Harry K. Messenger.

Verdaguer, J. **Thoughts on phorias.** Arch. chil. de oftal. **22-23**:27-30, 1949.

It is incorrect to associate heterophoria with the ocular muscle apparatus itself; it should rather be thought of with the supranuclear centers. Of the latter, the centers for convergence and divergence are the most important. Movements of fusion, in which the images of an external object falling upon a parafoveal area are transferred to the maculae, are executed with mathematical precision. A slight error in position produces diplopia. Movements which produce binocular vision are not purely reflex, for the cortex plays a role. The term "automatic" is preferred, recognizing the influence of the psychovisual centers of the occipital cortex. Auditory and labyrinthine controls play a role in fusion also. Imperfect movements of fixation are the basis of heterophoria. For diagnosis, the cover test, Maddox rod, near point of convergence, and prism vergence measurements are necessary.

Headache, not relieved by correction of refractive errors, and unexplained by other causes, is the most prominent symptom in the patient with heterophoria. The majority of patients have a neurotic character, making evaluation somewhat difficult. A therapeutic test is used in which one eye is occluded for ten days. Relief of symptoms is considered indicative of the association of the heterophoria and the

symptoms. Orthoptic training is highly successful in treating heterophorias. Results are best in convergence insufficiency, the most common of all anomalies of motility. Prism exercises are the only orthoptic therapy discussed.

James W. Brennan.

Villaseca, A. **New concepts on the pathogenesis and treatment of strabismus.** Arch. chil. de oftal. **22-23**:31-33, 1949.

Binocular vision appears postnatally in a sequence of various visual reflexes. First to appear at the age of three weeks is the reflex of monocular fixation, followed by that of conjugate fixation at four to six months. Shortly thereafter the reflexes of convergence and the corrective reflex of fusion develop. During the first five to seven years of life, these reflexes become conditioned in the cerebrum until they are almost automatic. If this normal development does not occur, the reflexes will never be developed. Therefore, strabismus is considered as a perversion of development of binocular reflexes. Any sensory, motor or central obstacle to development may provoke strabismus. One of three visual adaptations may result: 1. diplopia, 2. suppression, or 3. anomalous retinal correspondence. Treatment is predicated upon an exact diagnosis, which includes examination with the synoptophore. The importance of early treatment is stressed, particularly before the age of seven years, when binocular vision is completely developed. James W. Brennan.

7

CONJUNCTIVA, CORNEA, SCLERA

Belmonte Gonzalez, Nicolas. **A study of the aqueous in traumatic ulcers of the cornea.** Arch. Soc. oftal. hispano-am. **12**: 598-603, June, 1952.

An Amsler puncture and examination of the aqueous was performed in thirty cases of corneal ulcer. The examinations showed that in serpigenous nonperforating ulcer suppurative microorganisms were present in the anterior chamber. It was not possible to differentiate the cytologic or bacteriologic data of favorable and unfavorable cases so that this procedure could not be utilized for a prognosis. The use of aureomycin ointment was a significant improvement in therapy. In 119 cases recovery occurred without a dacryocystectomy or paracentesis of the anterior chamber, procedures which formerly were performed frequently in the treatment of serpigenous ulcers. Ray K. Daily.

Bjorkenheim, Barbro. **On precipitating factors in phlyctenular keratoconjunctivitis.** Acta ophth. 1951, Supplement 36.

The objective of this investigation was to elucidate the relation between phlyctenular keratoconjunctivitis, tuberculosis and other bacterial infections. The material consisted of 250 cases of phlyctenular keratoconjunctivitis and a control series of 51 cases of conjunctivitis and 9 of conjunctivitis with superficial keratitis. The report of the study is preceded by a review of the literature which shows that the allergic nature of phlyctenular disease is now generally accepted. It is also agreed that tuberculosis plays an important part in the pathogenesis of phlyctenular disease, and that a significant influence must be ascribed to the presence of streptococci and staphylococci. The author's material reveals a tuberculosis heredity in 58 percent of cases of phlyctenular disease; 98 percent of the patients were tuberculin positive, and their sensitivity was stronger than that of the controls. Clinical signs of tuberculosis were found in 62 percent. The antistreptococcus titer was elevated in 71 percent and in 17 percent of the controls. B-hemolytic streptococci were found in the throats of 42 percent of the patients and in only ten percent in the control series. The antistaphylococcus titer was elevated in 43 percent of the patients, and

in 22 percent in the controls. Mannite and coagulase-positive hemolyzing streptococci were found in the throats of 28 percent of the patients and 10 percent of the controls. It is concluded that the streptococcus and staphylococcus are factors in the genesis of phlyctenules. This conclusion is supported by the statistically verified beneficial effect of penicillin in these cases. Ray K. Daily.

Chinaglia, V. **Clinical and histologic study of a case of paramyloidosis of the bulbar conjunctiva.** Ann. di ottal. e clin. ocul. **78**:81-108, Feb., 1952.

Chinaglia reports a case of unilateral paramyloidosis (that is, a purely localized amyloid degeneration) of the bulbar conjunctiva occurring in a 47-year-old woman, and reviews various theories of etiology and pathogenesis. In this particular case no clinical evidence of any previous inflammation of the eye was found, but the histopathologic findings indicate a preceding nonspecific inflammatory process of unknown origin, whereby, with a mechanism likewise unknown, a localized alteration in protein metabolism resulted in paramyloidosis. (1 stereogram, 5 photomicrographs, references)

Harry K. Messenger.

Contardo, R. **Corneal ulcer due to Pseudomonas aeruginosa.** Arch. chil. de oftal. **22-23**:131-133, 1949.

A severe infiltrating corneal ulcer, which threatened loss of the eye, was resistant to penicillin, cauterization, sulfonamides and atropine. Many colonies of Pseudomonas aeruginosa (bacillus pyocyaneus) were cultured from the ulcer. After identification of the organism, streptomycin was administered both systemically and locally, with immediate improvement in the lesion and disappearance of the organism from the ulcer. Two months later, the eye had healed, although a large corneal opacity remained. A review of the literature indicates that corneal ulceration due to this organism is rare but most serious and may cause loss of the globe. Some strains are sensitive to streptomycin, some to sulfonamides, but none are sensitive to penicillin. The advisability of studying ocular infections bacteriologically is apparent. James W. Brennan.

Contardo, R., and Dubernet, J. **Treatment of rosacea keratitis with testosterone.** Arch. chil. de oftal. **22-23**:99-102, 1949.

Some patients who have allergic disorders are hypersensitive to their own hormones. Zondek and co-workers have shown that many patients with rosacea keratitis react to testosterone when injected intracutaneously in small doses. A positive reaction in women is due to the secretion by the adrenal cortex of a hormone analogous to testosterone. It is recognized that many other factors may play a role in the etiology of rosacea keratitis, and that spontaneous remissions occur, all of which makes evaluation of treatment difficult. It is felt that ariboflavinosis is not a factor in the etiology, although improvement follows administration of the vitamin. Treatment begins with subcutaneous injection of 0.05 mg. of the hormone, with a daily increase of 0.05 to 0.1 mg. until 1 mg. is reached. A pellet of 10 mg. is then implanted. Response to treatment is generally rapid if there is to be any benefit. Photophobia and lacrimation decrease, and corneal infiltrates and vascularity gradually diminish and disappear. The facial lesions may also improve. The author feels that his results are superior to those obtained with previous regimens, although his experience is limited to five patients with failure in one in whom the diagnosis was doubtful. Case histories are reported in detail. James W. Brennan.

Contino, Filippo. **The microchemical nature of trachoma. I. Piekarski-Robinow reaction of inclusion bodies.** Riv. ital. del

trac. e di pat. ocul. esot. **3**:39-45, April-June, 1951.

The Piekarski-Robinow reaction suggests that desoxyribonucleic acid is present and that the inclusion bodies are nucleoprotein. Contino emphasizes the importance of the blue staining by toluidine blue of the inclusion body which has been hydrolised by hydrochloric acid, a property it has in common with the elementary and the initial body as opposed to the red-violet staining of the nucleus of the host cells. Francis P. Guida.

Geraci, P. **Preliminary notes on the treatment of trachoma and other ocular disease with terramycin.** Riv. ital. del trac. e di pat. ocul. esot. **3**:55-58, April-June, 1951.

Terramycin hydrochloride ointment (1 and 2 percent) proved helpful in reducing conjunctival secretions in many corneal infections and in corneal pannus of trachomatous origin. It is of little value in papillary hypertrophy and has no effect on the trachomatous follicle.

Francis P. Guida.

Giardini, A. **The pathogenesis and therapy of rodent ulcer of the cornea.** Boll. d'ocul. **31**:193-205, April, 1952.

The author proposes the hypothesis of a toxic origin of rodent ulcer assuming that an allergic process is responsible for the production of the toxic substances. A 50-year-old man with bilateral rodent ulcer of the cornea underwent a great many different treatments without any relief; plesiotherapy and antiallergic treatment brought slight improvement. Conjunctival covering was tried repeatedly without success. A mucous membrane graft from the patient's lip, however, initiated a definite cure. It was transplanted so as to cover the corneal defect and to replace a large area of adjacent bulbar conjunctiva. (6 stereophotographs, references) K. W. Ascher.

Gormaz, A. **Chronic conjunctival tuberculosis treated with streptomycin.** Arch. chil. de oftal. **22-23**:121-124, 1949.

This is a detailed case report of a patient whose illness began twenty years previously with what probably was tuberculous dacryocystitis. After surgery on the lacrimal sac, epiphora, epistaxis, ulceration of the nasal mucosa, and nonspecific chronic conjunctivitis developed on the side which had been previously treated. A biopsy indicated verrucose tuberculosis of the conjunctiva. Response to usual therapy was poor, and epithelial keratitis developed, followed by ptosis, symblepharon, conjunctival ulceration, and corneal infiltration. Vision was markedly impaired. Streptomycin was administered locally in the form of eye drops, and was injected subconjunctivally and directly into the substance of the lesions. Novocain was added to the solution to be injected, but even that failed to eliminate the severe pain caused by the drug. Within a few days noticeable improvement was noted, both objectively and subjectively. Treatment was continued for several weeks when an ulcerative stomatitis developed which was attributed to the drug. A second course of streptomycin was administered after a rest of several months. The final result of treatment was highly satisfactory, with marked regression of the lesions and restoration of vision. Some scarring of the conjunctiva and cornea remained, but seems of little consequence.

James W. Brennan.

Grom, Edward. **Epithelial hyperplasia of the limbus.** Arch. Soc. oftal. hispano-am. **12**:404-409, April, 1952.

A primary hyperplasia, and one associated with an inflammatory process are reported. The literature on epithelial corneal hyperplasia is reviewed.

Ray K. Daily.

Hanser, S. A., Moor, W. A., and Stickle,

A. W. **Cytology of allergic conjunctivitis.** A.M.A. Arch. Ophth. **47**:728-733, June, 1952.

The findings in the examination of 572 conjunctival smears are analyzed. Patients with chronic conjunctivitis in whom no causative agent had been found and who showed a high eosinophile count in the conjunctival smear were selected. The patients showed an eosinophile count of 3 to 10 percent on scrape smear. Various therapeutic agents were tried. Cortisone locally or systemically produced a greater decrease in the eosinophile scrape smears and gave better subjective improvement than other agents used. The next most effective agent in producing a decrease in eosinophile count in smears was hypodermically administered staphylococcus toxoid. George S. Tyner.

Heer, G. **The cause of phlyctenular keratoconjunctivitis.** Rassegna ital. d'ottal. **21**:102-124, March-April, 1952.

Among the various etiologic factors considered in phlyctenular disease, primary importance is given to tuberculosis. In addition an intestinal auto-intoxication plays a part, for this favors the passage into the circulation of toxic substances not neutralized by the liver. It is this hepatic insufficiency which results in improper metabolism of fats. This latter is often expressed as an acetonuria. Several cases are reported confirming the author's observations. (3 figures, 45 references)

Eugene M. Blake.

Mata Lopez, Pedro. **Ocular complications of grippe.** Arch. Soc. oftal. hispanoam. **12**:587-596, June, 1952.

After an epidemic of grippe in January and February, 1951, Mata encountered ocular complications in 14 patients. Two had conjunctivitis, seven dendritic keratitis, and five atypical keratitis. In the latter the corneal lesions were superficial, paracentral, practically always in the temporal sector, and stained with fluorescein; the infiltrations were subepithelial and in severe cases extended into the superficial layers of the parenchyma. The keratitis was associated with severe conjunctival symptoms such as hyperemia, chemosis, lacrimation, photophobia, discomfort, and pain and a tendency to a serous iritis. The disease lasted about three weeks, and recovered under treatment with mydriatics, aureomycin and sulfacetamide. These lesions developed during the acute stage of grippe, while the dendritic keratitis developed during convalescence and was associated with labial or nasal herpes. A review of the literature on ocular complications of grippe shows that the question whether these complications are due to the virus of grippe or to a secondary agent still remains unsettled.

Ray K. Daily.

Pagani, M. **Some technical details in transplantation of the cornea.** Ann. di ottal. e clin. ocul. **78**:251-254, April, 1952.

Pagani's remarks apply only to perforating keratoplasties. In the absence of synechias he recommends mydriasis for small grafts and miosis for large. He uses a trephine and thinks it of no advantage to cut out the corneal disc in a single movement of the instrument. As soon as the trephine has perforated he gradually enlarges the opening, thus better protecting iris and lens. Great care must be taken to cut the endothelium and Descemet's membrane with an even unnotched edge in both host and graft. He covers cornea and graft with a disc of cellophane over which the stay sutures are placed. In the center of the disc is a 1.5 mm. opening for applying penicillin when the eye is dressed. Only in interstitial keratitis can success be expected if the cornea is vascularized. In other cases of vascularization previous treatment with beta radiation and with peritomies is advised. The refractive state of an eye after corneal transplantation is

hard to determine, but in any case contact lenses can be expected to give much better vision than ordinary glasses.

Harry K. Messenger.

Rapisarda, Dante. **Conjunctival organ therapy in trachoma.** Riv. ital. del trac. e di pat. ocul. esot. 3:119-143, Oct.-Dec., 1951.

Conjunctival organ therapy of trachoma consists of the implantation of a piece of fresh animal conjunctiva under the conjunctiva of a trachomatous patient. Six of 24 patients were cured, thirteen were improved, and five were unaffected. These results were better than those obtained by subconjunctival injections and by topical therapy. The principle of this treatment is based on 1. the viral nature of the etiologic agent of trachoma, 2. local antitrachomatous immunity, and 3. the possibility of the transference of hypothetic antiviral principles present in animal conjunctiva to the human conjunctiva. The procedure is harmless. Experiments suggest that penicillin therapy would strengthen the organ-therapy reaction.

Francis P. Guida.

Sakic, Dinko. **Serpiginous corneal ulcer and its treatment by catholysis.** Ann. d'ocul. 185:618-631, July, 1952.

Two hundred and seventy cases of corneal ulcers are statistically analyzed as to ages and vocations of the patient, infective organism and the results of treatment. Most of the patients were farmers, men, 30 to 50 years old. The bacteriologic data are not accurately described but apparently the most frequent causative organisms were staphylococcus, streptococcus, and pneumococcus. Atropine, sulphamides and antibiotics, as well as the author's catholysis were the principal methods of treatment employed. In the last-named procedure a dilute peroxide hydrogen solution is repeatedly applied to the ulcer with a needle attached to the negative pole of a 3 to 4 ma. current. Gentle applications are made during a 10 to 15 second period and may be repeated in 24 to 48 hours if necessary. They are frequently followed by slight bullae in the superficial cornea which are due to the deposit of the OH radical in the ulcer tissue. The author prefers his method of treatment to the others employed. Chas. A. Bahn.

Tsutsui, Jun. **Low virulent trachoma and the tumor-like nature of late trachomatous change.** Acta Soc. Ophth. Japan 56:712-716, Aug., 1952.

The author summarizes a series of his previous reports on trachoma as follows: 1. inoculations with inclusion-negative material fail to produce trachoma in general, 2. inclusion-negative materials do not give virus shadow in the electron micrograph, 3. in inclusion-negative cases, Mitsui's mechanical provocative test fails, while it does not fail in inclusion-positive cases, and 4. chemotherapy is more effective in inclusion-positive cases than in negative cases. Thus he claims the existence of "low virulent trachoma," and he considers the morbid changes in such cases to be of a tumor-like nature rather than an inflammation. He further refers to an increase in anaerobic glycolysis in such conjunctivae, which he considers to be characteristic of tumor-like tissues.

Yukihiko Mitsui.

Weekers, L. **Changes in the cornea due to local medication with sulfamides and antibiotics.** Ann. d'ocul. 185:549-551, June, 1952.

That sulfamides and antibiotics kill only the bacteria and leave the tissues unharmed is an erroneous supposition. Local treatment with these drugs shows marked changes in the corneal epithelium. In corneal ulcers, for example, trying one antibiotic after another when the diseased condition is not healing often aggravates the lesion. These drugs must be discon-

tinued when their primary work is done. Healing is aided by removal of the dead epithelium with cotton soaked in ether. The type of lesion described is not seen when treatment is by drugs other than antibiotics. B. T. Haessler.

Zeppa, Rosario. **Large dosages of penicillin in trachoma.** Riv. ital. del trac. e di pat. ocul. esot. **3**:23-28, Jan.-March, 1951.

A comparison of groups of patients using penicillin by mouth, penicillin with sulfa drugs, and sulfa drugs alone, suggests that penicillin is of no specific value in trachoma. It did, however, seem to control the secondary invading organisms.

Francis P. Guida.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Brognoli, C. **Two cases of progressive choroidal atrophy.** Ann. di ottal. e clin. ocul. **78**:259-268, April, 1952.

Brognoli presents detailed case reports of typical bilateral essential (gyrate) atrophy of the choroid occurring in two brothers, aged 49 and 45 years. There was no parental consanguinity. In the elder brother, who had 4D of myopia and whose vision was reduced to hand movements, the atrophy was complete except in a few small peripheral areas and in a zone at the macula. The emmetropic younger brother, with 20/40 vision and with concentrically contracted fields, was anomalous in not being night blind. The principal theories of pathogenesis are discussed. Brognoli would place the primary lesion in the choroidal vessels. (References)

Harry K. Messenger.

Gilbert, W. **The pathology of the uvea, especially ophthalmia lenta.** Arch. f. Ophth. **152**:399-412, 1952.

The author reviews numerous factors which might be involved in the pathogenesis of diseases of the uvea. In many cases the etiology remains unknown. However, in some instances of so-called ophthalmia lenta clinical and serological studies demonstrated conditions produced by various types of leptospirae. Other authors had shown the presence of leptospira canicola in the aqueous of a horse with cyclic uveitis, a condition closely related to man's ophthalmia lenta. A leptospirosis should be considered in cases of otherwise unknown etiology.

Ernst Schmerl.

Gonzales-Pola, A. M., and Magdalena Castineira, J. **Two cases of sympathetic ophthalmia.** Arch. Soc. oftal. hispano-am. **12**:575-586, 1952.

Two cases of sympathetic ophthalmia which in spite of all therapeutic efforts ended in blindness are reported. After some reference to the literature the authors present a hypothesis on the pathogenesis of sympathetic ophthalmia. Essentially they believe that it is characterized by structural changes, dependent upon changes in the midbrain, and that it is the influence of the central nervous system which is responsible for the pathologic processes of sympathetic ophthalmia. The authors maintain that true sympathetic ophthalmia is a very rare disease, and are critical of the report made by Barraquer of 17 cases encountered within a period of one and one half years. They are also sceptical of the reported beneficial results of therapy, and believe that many cases of reported sympathetic ophthalmia were in reality cases of iridocyclitis.

Ray K. Daily.

Gonzales-Pola, Angel Moreu. **The problem of non-specific uveitis.** Arch. Soc. oftal. hispano-am. **12**:469-492, May, 1952.

The author presents a theory of the pathogenesis of non-specific uveitis, based on Selye's adaptation syndrome, Klemperer's collagen syndrome and Speranski's

neurogenic theory. The absence of clinical signs indicative of the etiology of uveitis is due to the fact that the process in the uvea is produced by bacterial foci in distant areas which affect the endocrine and neurovegetative metabolism. The effect of cortisone and ACTH on the uveal processes and on the relation of hyaluronidase to hyaluronic acid is discussed.

Ray K. Daily.

Haik, G. M., Waugh, R. L., Jr., and Lyda, W. **Sympathetic ophthalmia.** A.M.A. Arch. Ophth. **47**:437-453, April, 1952.

The authors present a review of the literature, a discussion of the subject, and reports one case. It has generally been accepted that the histologic changes of sympathetic ophthalmia are similar in the "exciting eye" and the "sympathizing eye." The authors studied a case of clinical sympathetic ophthalmia which occurred four weeks after an extracapsular cataract extraction in a 68-year-old patient. The "sympathizing" eye was enucleated. The histologic findings were those of endophthalmitis rather than the classic findings of sympathetic ophthalmia. The authors believe this patient had bilateral endophthalmitis phacoanaphylactica and that the two diseases are frequently confused. It is important to differentiate the two diseases because endophthalmitis phacoanaphylactica is treated by removal of lens remnants in the operated eye and intracapsular lens extraction in the unoperated eye. Corticotropin and cortisone are valuable adjuncts to therapy but do not make antibiotics, mydriatics and other supportive treatment unnecessary. (5 figures, 27 references) George S. Tyner.

Ikui, H., Hiroishi, M., and Furuyoshi, Y. **Histopathology of idiopathic uveitis of Vogt-Koyanagi, a report of two cases.** Acta Soc. Ophth. Japan **56**:1079-1091, Sept., 1952.

In two cases of Vogt-Koyanagi's syndrome, the eyeball was removed five and 11 months after the onset of the disease. Nodular nests of lesions were found in the choroid. The center of the nodules consisted of epithelioid cells which contain melanin granules, surrounded by a wall of plasma cells and lymphocytes. The lesions are apt to localize in the outer layer of the choroid and no chromatophores are found in the inner layer of the choroid. The authors consider the finding to be the same as those found in sympathetic ophthalmia. They tried to find a viral agent without success. Discussion of the report was opened by Sugiura, who had isolated and mantained a virus in mouse brain from an early case of Harada's disease. The identification of the virus had not yet been conclusive, but the virus had caused a severe uveitis when inoculated into rabbit vitreous.

Yukihiko Mitsui.

Malatesta, C. **Bilateral uveitis with retinal detachment, alopecia and poliosis.** Boll. d'ocul. **31**:221-232, April, 1952.

A woman, aged 34 years, showed a combination of Vogt-Koyanagi's and Harada's syndromes. At the onset she had general malaise, headache, and loss of appetite. Treatment consisted of the administration of foreign protein, streptomycin, aureomycin, and blood transfusions. After two months the bilateral retinal detachment had disappeared, the vitreous body seemed clear, the iridocyclitis had subsided and large areas of depigmentation appeared in both fundi. The author stresses the close relationship between Harada's and Vogt-Koyanagi's syndromes. (References)

K. W. Ascher.

Nano, H., and Saba, J. **Iridocyclitis with intercurrent hypopyon.** Arch. de oftal. de Buenos Aires **26**:505-509, Nov., 1951.

A white man, 25 years old, developed intercurrent iridocyclitis with hypopyon

after brucellosis. During the acute stage of the brucellosis he had symptoms of a mild bilateral iridocyclitis. In the subsequent months he had a severe iridocyclitis in one eye or the other every two months. Two years later he was seen at the clinic with another severe attack of iridocyclitis with a large hypopyon in the right eye. The pus in the anterior chamber was not examined because it had almost disappeared the day after treatment was instituted. The left eye developed a similar condition two months after recovery of the right eye. Vision in both eyes returned to normal. The uveal reaction was probably due to an allergic manifestation to the brucella organism and not a direct action of it. Jose F. Pietri.

Pineri y Carrion, A. **Etiology of iridocyclitis.** Arch. Soc. oftal. hispano-am. **12**: 300-340, March, 1952.

A comprehensive review of the literature is presented. Ray K. Daily.

Redslob, E. **Dr. Schreck's recent important studies on the pathogenesis of sympathetic ophthalmia.** Ann. d'ocul. **185**: 558-563, June, 1952.

Redslob considers the work that Schreck has done during the last 20 years of the greatest importance. Schreck divides sympathetic disease into two groups, the retinal and the choroidal type, with distinct pathologic processes but the same fundamental course and etiology. An ultramicroscopic virus with an affinity for uveal tissue is the causative agent. It travels from the first eye along the retinal vessels, continues as a periangiitis or perineuritis up into the chiasm, and reaches the second eye by way of the opposite optic nerve (always as a periangiitis). The infiltrations become less on their way up the first optic nerve, but at the chiasm they pile up in masses. Going down the second nerve they increase in volume and are distributed along the uvea of the second eye. During this course from eye to eye the inflammatory process keeps its primary characteristics; if the infiltration contained epithelial and giant cells in the interior of the globe, they occur equally in the extraocular infiltrations. The most marked infiltration is found in the perivascular spaces of the anterior uvea. Schreck believes that the organisms have a special affinity for intraocular lymph, and an aversion for the lymph of the central nervous system, for which reason the brain is never affected by this virus as it sometimes is by the virus of herpes.

In 1948 Schreck demonstrated microorganisms, rickettsial in character along the optic nerves and chiasm. He considered them to be lymphotropic and migratory rickettsias. He was able to obtain the organism from either uvea or aqueous of either the sympathising or the primarily affected eye of man or fowl. The organism can be transmitted into a human or into a chicken eye by inoculation into the anterior chamber or vitreous, or by lightly scratching the lens. A temperature of 37° C and absolute sterility must be maintained. Repeated animal passage increased the virulence although some chickens as well as rabbits and pigeons develop immunity. Material from infected chicken eyes produced a uveitis identical with that of sympathetic ophthalmia. It could be followed from one eye to the other as a migratory periangiitis across the optic nerves and chiasm.

Schreck has cultivated the organism on the chorioallantois of incubated chicken eggs. If shreds of uvea are added during 12 to 14 days, the organisms multiply in the uveal tissue. They then invade the ectodermal layer of the allantois and produce a migratory periangiitis. The organisms can be cultivated from allantois to allantois in multiple series and finally reinoculated into the chicken eye to again produce the disease. Eyes of monkeys

have been similarly inoculated. Morphologically the "sympathetic rickettsia" resembles a coccus. It stains violet with Giemsa and is Gram positive. Schreck suggests the inoculation of the allantois with material from an eye in which sympathetic disease is suspected as a diagnostic procedure. If present, the organisms will multiply. Therapeutically the use of penicillin and streptomycin are harmful as they kill the accessory flora and give free rein to the germ of sympathetic ophthalmia. B. T. Haessler.

Roda Perez, E. **Nitrogen mustard in the treatment of uveitis of undetermined etiology.** Arch. Soc. oftal. hispano-am. **12**: 132-149, Feb., 1952.

In five cases of severe uveitis, in which there was no response to the usual forms of therapy, nitrogen mustard was effective. The cooperation of an internist is essential in the administration of this drug. Its deleterious effects on red blood cells is combatted by blood transfusions and the administration of the myelogenous stimulants, liver extract and vitamin B 2. The patient should be on a high protein diet during the treatment and for a time thereafter, as the leukopenia induced by nitrogen mustard persists for a time after the treatment has been discontinued. Since it does not have any effect on the etiologic agent, nitrogen mustard does not prevent recurrence. Ray K. Daily.

Wilder, H. C. **Toxoplasma chorioretinitis in adults.** A.M.A. Arch. Ophth. **47**: 425, April, 1952.

Organisms having the characteristics of toxoplasma were identified in chorioretinal lesions in 41 eyes removed from patients between the ages of 16 and 72 years. The lesions were uniform in type, granulomatous with marked necrosis.

George S. Tyner.

9

GLAUCOMA AND OCULAR TENSION

Frey, W. G., and Posner, A. **Familial glaucoma.** A.M.A. Arch. Ophth. **47**:454-458, April, 1952.

A pedigree of a family with glaucoma simplex in four generations showing dominant inheritance is reported. The glaucoma begins at an early age and is favorably influenced by early operation, trephination. The disease did not differ from the usual adult chronic simple glaucoma.

George S. Tyner.

Hara, Kiyoshi. **Influence of epinephrine and acetylcholin on the pulsation curve of intraocular tension.** Acta Soc. Ophth. Japan **56**:883-890, Aug., 1952.

The pulsation curve of the ocular tension was measured by means of an unusual elecromanometer and with a differential calculus amplifier. When epinephrine was injected subconjunctivally, the curve showed changes corresponding to those which occur in bloodvessels of the other parts of the body when they contract. The changes occurred one to five minutes after an injection and lasted for 60 to 100 minutes. When acetylcholin was used, a dilation of the intra-ocular blood vessels was brought about immediately after the injection; it reached the climax in four to eight minutes and lasted for about 20 minutes. The author emphasizes the fact that a change in the ocular tension was brought about parallel to the dilatation or to the contraction of the intraocular bloodvessels. Yukihiko Mitsui.

Ono, Yasuharu. **Gonioscopic study of Schlemm's canal after eyeball compression.** Acta Soc. Ophth. Japan **56**:905-922, Aug., 1952.

In 81 normal eyes, after compression of the eyeball at 150 gm. for 10 minutes, 27-percent lowering of the intraocular tension resulted on the average. A gonioscopic

examination revealed a red coloration at the sclerocorneal trabeculum, without exception, after the cessation of the compression. In six glaucomatous eyes, the average lowering of the ocular tension was only 3 percent after the compression. In none of the cases was the red coloration observed by gonioscopy at the end of the compression. The author considers a combination of the compression test and gonioscopy to be encouraging in the early diagnosis of glaucoma.

Yukihiko Mitsui.

Pagliarani, N. **Glaucoma in high myopia.** Boll. d'ocul. **31**:257-270, May, 1952.

Fifty eyes with high myopia and extensive chorioretinal atrophy were subjected to the caffein test, water-drinking test, and combined lability test. Careful plotting of the visual field and graphing of the diurnal pressure variations with and without miotics were performed. Four of fifty eyes were found to have glaucoma; in many others, some of the provocative tests suggested its possible presence. Every highly myopic eye should be carefully studied to rule out glaucoma. (2 figures, 1 table, 34 references)

K. W. Ascher.

Probert, L. A. **A survey of hereditary glaucoma.** Canad. M.A.J. **66**:563-568, June, 1952.

All patients in Ontario, registered with the Canadian National Institute for the Blind for the years 1918-1949, were studied in an attempt to establish the hereditary factor in glaucoma. Of the 832 registered cases of glaucoma 571 had primary glaucoma and of these, 102 had a hereditary history. The incidence of hereditary glaucoma from this series was 17.8 percent. Glaucoma may be inherited as a dominant or as a recessive character. In contradistinction to belief that most inherited glaucoma is of the juvenile type, occurring before the age of 35 years, the average age of onset in this series was 56 years, or only four years earlier than that of primary nonhereditary glaucoma. Anticipation did not occur. Two-thirds of the cases of hereditary glaucoma were of the chronic congestive type. The type was usually constant in a pedigree, but mixing of types was observed. No linkage of eye color, hair color, blood groups or the ability to taste phenylthiocarbamide was observed. No evidence of any relationship between adult glaucoma and hydrophthalmos was found. No case of proved hydrophthalmos was found to occur in families of adult glaucoma, and in 36 families in which hydrophthalmos occurred, no case of adult glaucoma was found.

Martin Ackerman.

Suda, Keiu. **Early diagnosis of glaucoma.** Acta Soc. Ophth. Japan **56**:933-958, Sept., 1952.

In 85 cases of glaucoma of various types, the author applied all of the diagnostic tests which have appeared in the literature and the data are summarized in 38 tables and in four figures. He found a "compression test" to be excellent in the diagnosis of glaucoma and he recommends the following procedure. A 50-gm. compression is applied to the eyeball for 10 minutes. After such compression, the lowering of the ocular tension is small in glaucomatous eyes, and immediately after the end of the compression the tension is from 7.9 to 33.3 mm. Hg, while in normal eyes the final tension is less than 7.0 mm. Hg, in most cases less than 4 mm. Hg. A greater or smaller compression than that given above does not give such a sharp contrast. After the compression, the blind-spot becomes more than doubled in diameter in glaucomatous eyes while the enlargement is very small in normal eyes. A red test object and 20 lux illumination give the best contrast. Yukihiko Mitsui.

10

CRYSTALLINE LENS

Bellows, J. S. **Lens and vitreous.** A.M.A. Arch. Ophth. **47**:516-537, April, 1952.

The publications which appeared in 1950 and 1951 are reviewed. (122 references) George S. Tyner.

11

RETINA AND VITREOUS

Bisland, T., and Topilow, A. **Subhyaloid hemorrhage and exophthalmos due to ruptured intraventricular aneurysm.** A.M.A. Arch. Ophth. **47**:470-476, April, 1952.

This is an interesting case report of the ocular and other signs of a massive subarachnoid hemorrhage due to rupture of a "berry" aneurysm of the third ventricle. The antemortem ocular signs were chemosis, proptosis, retinal hemorrhages, and congestion of the retinal veins of the right eye, and a massive subhyaloid hemorrhage of the left eye. Photomicrographs of the subhyaloid hemorrhage, taken from sections of the globe postmortem, show that the hemorrhage was between the internal limiting membrane of the retina and the nerve fiber layer. The cause of the proptosis was an orbital hemorrhage extending from the apex of the orbit and surrounding the optic nerve. (3 figures, 18 references) George S. Tyner.

Hirose, Toichiro. **Electroretinogram in night blindness.** Acta Soc. Ophth. Japan **56**:732-741, Aug., 1952.

In congenital or hereditary night blindness, such as Oguchi's disease, pigmentary degeneration of the retina and retinitis punctata albescence, the b-wave was invariably absent in the electroretinogram.

In night blindness accompanied by acquired neuroretinal disorders, a small but typical b-wave was observed in some instances. Yukihiko Mitsui.

La Rocca, V. **Retinal detachment from di-isopropyl fluorophosphate in an aphakic eye.** New York St. J. M. **52**:1329-1330, May 15, 1952.

Complete retinal detachment in an aphakic eye occurring a few days after the use of D.F.P. for a secondary glaucoma following cataract extraction is reported. A theory is advanced that the formation of the detachment is due to two factors: spasm of the meridional ciliary muscle fibers which pull on the choroid and the transudation of plasma as a result of the congestion of the choroidal vessels, which loosens the adhesiveness between the choroid and the retina and facilitates the detachment. Martin Ackerman.

Lijo Pavia, Justo. **A rare tapeto-retinal degeneration of the macula with the appearance of luminescent crystals.** Rev. oto-neuro-oftal. **27**:27-36, 51-60, 1952.

Four cases are described and illustrated. The lesion was always bilateral, situated in the macula and characterized by the presence of numerous glistening crystals, probably cholesterol. The central vision was greatly impaired. Only one patient had a family history of similar eye troubles, but this could not be verified. Two patients had hypercholesteremia and all four of them showed choroidal degeneration in the macular area. All patients had defective color vision and decreased dark adaption. The author gives a survey of cases described as cholesterol degeneration of the macula. He regards this type as an acquired degeneration. He discusses the possibility of a lipoid degeneration of choroidal drusen. Frederick C. Blodi.

Swan, K. C., and Hyman, S. **Experiences with tumors of the retina.** A.M.A. Arch. Ophth. **47**:416-424, April, 1952.

This is the fourth in a series of reports concerning experiences of the authors with tumors of the eye and adnexa. Post-

inflammatory or post-traumatic proliferative and cystic conditions simulating retinal neoplasms, metastatic tumors of the retina, and the phacomatoses with retinal involvement are comparatively rare. The incidence of retinal lesions secondary to choroidal tumors is to be discussed in a later publication.

The commonest primary neoplasm of the retina observed was retinoblastoma which seemed to arise from undifferentiated or poorly differentiated primitive cells. Most of the report concerns a discussion of 25 patients with retinoblastoma observed during the past seven years. Although this is statistically a small series, some interesting facts are brought out. 1. In only one of 20 cases completely followed was there a history of retinoblastoma in a second member of the family. 2. In 12 of 20 patients the lesion was bilateral. 3. Over half of the eyes showed histologic evidence of extraocular extension of the tumor. 4. One eye almost always was involved earlier than the other. 5. Early diagnostic signs are difficult to recognize but in children with strabismus, pupillary inequality, and differences in size of the globes neoplasm should be searched for. The "cat's-eye-yellow" reflex is a rather late sign. 6. Differential diagnosis is relatively easy because the ocular media remain clear and the lesion has typical features, such as a focal loss of transparency of the retina or an isolated tumor mass or masses appearing "ghostly" white. 7. Many retinoblastomas transilluminate well. X-ray evidence of calcification is a reliable sign and occurred in 18 of 23 eyes examined. The presence of calcium, however, should not be considered a pathognomonic sign. 8. No patient with monocular tumor had useful vision in the affected eye. Enucleation with excision of the orbital portion of the nerve was the treatment of choice. Exenteration or postoperative irradiation or both were reserved for patients with histologic evidence of extrabulbar extension. In bilateral cases, enucleation of the most advanced eye and irradiation by the Reese-Martin technique of the other eye was done. (3 figures, 5 references)

George S. Tyner.

14

EYEBALL, ORBIT, SINUSES

Levi, M., and Salvi, G. L. **Ophthalmoplegia in Graves' disease evolving into malignant exophthalmos.** Boll. d'ocul. **31**: 291-306, May, 1952.

Early in the course of Graves' disease, a 49-year-old woman developed chemosis, palpebral edema and paralysis of her right superior rectus muscle. Thiuracil treatment was instituted and when the basal metabolism became normal, a marked bilateral exophthalmos developed, which was accompanied by paralysis of elevation and transient retrobulbar neuritis in first the right eye, then in the left. The pathogenesis of malignant exophthalmos is discussed. (2 figures, references)

K. W. Ascher.

17

INJURIES

Brockhurst, R. J. **Intraocular rubber foreign bodies after surgery.** A.M.A. Arch. Ophth. **47**:465-469, April, 1952.

Seven cases are described in which bits of rubber were seen in the eye after surgical operation. The rubber is apparently well tolerated. Its source was a cemented rubber bulb attached to the anterior chamber irrigator. (5 figures, 4 references)

George S. Tyner.

Le Win, T. **Teaspoon penetrating child's orbit.** A.M.A. Arch. Ophth. **47**:515, April, 1952.

A case report of a 19-months-old child with a penetrating injury of the orbit

from the handle of a teaspoon is presented to emphasize the importance of antibiotics in the management of injuries and because of the rarity of the type of injury. (2 figures in color) George S. Tyner.

18

SYSTEMIC DISEASE AND PARASITES

Jacobs, A. A. **Congenital ocular toxoplamosis.** New York St. J. M. **52**:1322-1323, May 15, 1952.

Infection with toxoplasma parasites can produce a variety of clinical syndromes in man, classified as follows: 1. congenital encephalomyelitis of the newborn, 2. acute encephalitis of children, 3. a typhus-like syndrome in adults associated with pneumonitis, 4. an acute febrile illness in adults similar to trichinosis, and 5. nonapparent infections in adults detected by finding circulating antibodies against the parasite. A history of the onset of signs and symptoms early in life, chorioretinitis, cerebral calcification and mental deficiency or psychomotor retardation commonly characterize congenital toxoplasmosis. In the acquired disease there is complete absence of ocular lesions. Fatal cases of toxoplasmic encephalomyelitis are characterized chiefly by convulsions, internal hydrocephalus, cerebral calcification, and chorioretinitis. A positive serologic reaction in high titer, which diminishes as time goes by, is the rule in toxoplasma infections. A case of nonfatal congenital toxoplasmosis in the inactive phase in a 12-year-old white boy is presented. The patient showed bilateral chorioretinitis which involved the macular area and some optic atrophy but there was an unusual absence of demonstrable intracranial abnormality and mental retardation. Martin Ackerman.

Quintieri, C. **Ocular changes in Hodgkin's disease.** Boll. d'ocul, **31**:307-14, May, 1952.

A 51-year-old woman with Hodgin's disease developed unilateral sector-like conjunctival hyperemia with superficial corneal infiltration near the limbus above and corresponding vascularization of the corneal periphery. Local therapy was of no avail but roentgen treatment (dosage not mentioned) improved both the general condition and the ocular affection. Biopsy from the limbal conjunctiva revealed atypical inflammatory changes. (4 figures, 25 references) K. W. Ascher

NEWS ITEMS

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News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received at least three months before the date of occurrence.

Announcements

Wills clinical conference

The fifth annual clinical conference of the staff and ex-residents of the Wills Eye Hospital will be held on March 20 and 21, 1953.

The Arthur J. Bedell Lecture will be delivered by Dr. John H. Dunnington of New York City.

Continuation course

The University of Minnesota will present a continuation course in ophthalmology for specialists at the Center for Continuation Study from January 19 to 24, 1953. Emphasis will be placed throughout the session on therapy of a variety of ocular disorders.

The visiting faculty for the course will include Dr. Kenneth C. Swan, professor and head, Department of Ophthalmology, University of Oregon Medical School, Portland. The course will be presented under the direction of Dr. Erling W. Hansen, professor and director, Division of Ophthalmology, and the remainder of the faculty will include members of the staff of the University of Minnesota Medical School and the Mayo Foundation.

Call for papers

The annual meeting of the Section on Ophthalmology of the A.M.A. will be held jointly with the Association for Research in Ophthalmology in New York City during the first week in June, 1953. The scientific exhibit of A.M.A. will run concurrently at the Grand Central Palace.

Titles and full abstracts of papers submitted for presentation at the meetings of the section should be in the hands of the secretary, Dr. Trygve Gundersen, not later than January 1, 1953. This is necessary in order to permit selection of papers and to make necessary arrangements for their competent discussion.

Papers of a technical nature are better submitted to the Association for Research in Ophthalmology. The winter sectional meeting of the association will be held this year in Baltimore. Early submission of material is prerequisite for its inclusion in the program.

The scientific exhibit will entertain presentations of a purely ophthalmological nature, but would prefer to have material of interest also to the general practitioner. An exhibit in conjunction with a paper read before the section is of particular interest. The material can be either of a research or instructional nature.

Inquiries regarding the above may be addressed to:

Section on Ophthalmology: Trygve Gundersen, M.D., 101 Bay State Road, Boston 15, Massachusetts.

Association for Research: Hunter H. Romaine, M.D., 111 East 65th Street, New York 21, New York.

Scientific Exhibit: William F. Hughes, Jr., M.D., 1853 West Polk Street, Chicago 12, Illinois.

Miscellaneous

Adjustment to aphakia

Type for the editorial, "Adjustment to aphakia," which appeared in the January, 1952, issue of the Journal, is still standing. Anyone wishing to purchase reprints should send an order at once to Miss Scilda Frick, George Banta Publishing Company, Menasha, Wisconsin.

Back issues wanted

The Journal has received requests for the following issues: February, 1948; February and July, 1950. Will anyone wishing to sell these issues, please write to the Ophthalmic Publishing Company, 664 North Michigan Avenue, Chicago 11, Illinois?

Research laboratories dedicated

Formal dedication of the Department of Research Laboratories of the Wills Eye Hospital took place at the hospital on October 7th. The three-story colonial structure which is fully equipped for ophthalmic research is located directly behind the hospital.

Ernest T. Trigg, vice-president of the Board of Directors of City Trusts, and chairman, Committee on Wills Eye Hospital, presided at the dedication ceremony. The Right Rev. Oliver J. Hart, D.D., Episcopal bishop, Diocese of Pennsylvania, pronounced the invocation. The principal address was delivered by former Associate Justice of the U. S. Supreme Court, Owen J. Roberts.

Other brief addresses were given by John A. Diemand, president, board of directors of City Trusts; Michael J. Byrne, deputy to the mayor of Philadelphia; Dr. Edmund B. Spaeth, president, the hospital's board of attending surgeons; Dr. Irving H. Leopold, director, Department of Research; and William C. Brown, secretary, Pennsylvania State Department of Welfare.

Approximately 300 persons, including city and state officials, attended the event which marked a milestone of achievement in the long history of the Wills Eye Hospital which, since its establishment in 1832, has been dedicated solely to the prevention of blindness.

Societies

Argentina congress

At the fifth Argentina Congress of Ophthalmology to be held during May, 1953, the official subject for discussion will be "Glaucoma." The Society of Ophthalmology of Litoral will present "Glaucoma: Its medical treatment," with Dr. Juan A. Maggi Zavalia, Dr. Juan M. Vila Ortiz, and Dr. Enrique V. Bertotto leading the discussion. The Ophthalmological Society of Cordoba will present "Chronic simple glaucoma."

Papers on glaucoma will be given by: Dr. Magin A. Diez, "Glaucoma: A social problem"; Dr. Jose A. Sena and Dr. Federico Cerboni, "Secondary glaucoma"; Dr. Federico K. Cramer, "Congenital glaucoma"; Dr. Jorge Balza, "The surgical treatment of glaucoma."

Dr. Hector Erausquin, "Acute glaucoma"; Dr. Edagardo Manzitti, "Hypertensive uveitis"; Dr. Rodolfo Lienau and Dr. Carlos Dellatorre, "Acute glaucoma from injection of air into the anterior chamber"; Dr. Eduardo Manes and Dr. José M. Paunessa, "Buphthalmos."

Dr. Orlando Travi and Dr. F. Belloward Ezcurra, "Glaucoma in phacomatosis"; Dr. Rodolfo Lienau and Dr. German Rillo Cabanne, "Posterior sclerotomy in acute glaucoma"; Dr. Roberto F. Pereira, "Surgical treatment of chronic glaucoma"; Dr. M. Marin Amat, "New concepts of the pathogenesis and treatment of glaucoma."

Dr. A. Magitot, "Ocular hypertension and primary glaucoma"; Dr. C. Espildora Luque, "Problems in glaucoma operations"; Dr. Jean Sedan, "The nervous symptoms of glaucoma"; Dr. A. Torres Estrada, "The pathogenesis of the glaucomatous excavation"; Dr. Esteban Adrogue and Dr. Alfonso Arrechea, "Results obtained in the treatment of chronic glaucoma."

Dr. José Maria Roveda, "The mechanism of action in antiglaucoma operations"; Dr. Moacyr Alvaro, "Results in a glaucoma clinic"; Dr. G. B. Bietti, "Progress in glaucoma diagnosis"; Dr. Carlos Pereira, "Clinical histories in glaucoma"; Dr. Olga Ferrer, "Familial glaucoma"; Dr. Justo Lijó Pavia, "Surgical treatment of glaucoma: Cyclodiathermy"; Dr. Rodolfo G. Ollé and Ruperto Ramirez, "Glaucoma and diabetes"; Dr. Rodolfo G. Ollé, "Iridencleisis."

Dr. Raul Cambiasso, "Late infections following the Elliot operation"; Dr. Paulina Santanowsky, Dr. Moises Brodsky, and Dr. Pedro Kurlat, "Preglaucoma"; Dr. Virgilio Victoria and Dr. Carlos Gordillo, "Retrociliary diathermy in the treatment of glaucoma: An interpretation of its mechanism."

Among other papers to be presented will be: "Cycloscopy," Dr. Esteban Adrogue and Dr. Hector Erausquin; "Ocular leprosy," Dr. Maximo Carlos Soto; "Hypertension in one eye," Dr. Rodolfo G. Ollé and Dr. Ruperyo Ramirez; "Experiences with dacryocystotomy," Dr. Rodolfo G. Ollé and Dr. Humberto Cortese; Dr. Hector Nano, "Hoffman's operation."

V Pan-American congress

The V Pan-American Congress of Ophthalmology will be held in Santiago, Chile, in February, 1956. The Chilean Ophthalmological Society has elected the following committee for arrangements: President, Dr. Cristóbal Espildora; vice-president, Dr. Santiago Barrenechea; secretary general, Dr. René Contardo; treasurer, Dr. Abraham Schweitzer.

For complete information, address the secretary general: Dr. René Contardo, Huérfanos 930, Of. 74, Santiago, Chile.

Reading meeting

At the 128th meeting of the Reading (Pennsylvania) Eye, Ear, Nose, and Throat Society, Dr. Arthur A. Bobb, Dr. Paul C. Craig, Dr. John J. Penta, Dr. Benjamin F. Souders, Dr. Harold L. Strause, and Dr. John M. Wotring reported the highlights of the 1952 meeting of the American Academy of Ophthalmology and Otolaryngology.

Personals

Dr. Trygve Gundersen, Boston, has been appointed professor of ophthalmology and head of the Department of Ophthalmology at Boston University Medical School.

Dr. Algernon B. Reese, New York, was guest speaker at the November 20th meeting of the Kansas City Society of Ophthalmology and Otolaryngology. Dr. Reese discussed "Newer aspects of glaucoma treatment," and "Practical points in ophthalmology," and showed the motion picture on the "Krönlein operation."

Dr. Hermann M. Burian, Department of Ophthalmology, State University of Iowa, Iowa City, has been appointed editor of the American Orthoptic Journal to succeed the late Dr. Richard G. Scobee.

Dr. Francis Heed Adler, Philadelphia, presented the 15th annual de Schweinitz Lecture before the Section on Ophthalmology, College of Physicians of Philadelphia, on November 20. The subject of Dr. Adler's address was "Pathologic physiology of strabismus."

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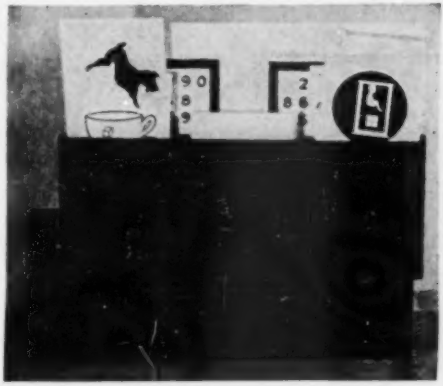

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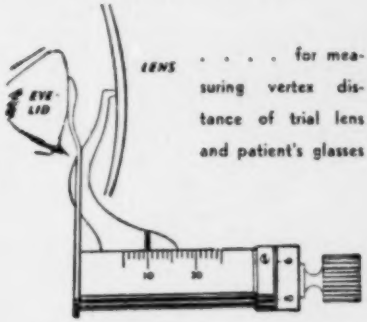

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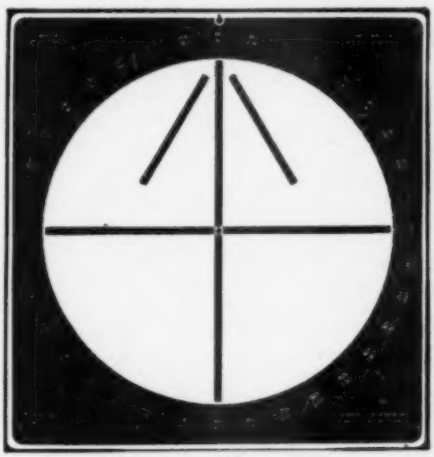

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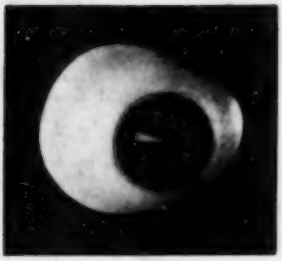

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